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BRITISH MEDICAL JOURNAL

LONDON SATURDAY JUNE 17 1950

STRESS AND THE GENERAL ADAPTATION SYNDROME*

BY

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With the concept of the general adaptation syndrome we have attempted to integrate a number of seemingly quite unrelated observations into a single unified biologic system. I would draw attention briefly to the work of Claude Bernard, who showed how important it is to maintain the constancy of the "*milieu intérieur*"; Cannon's concept of "homoeostasis"; Frank Hartmann's "general tissue hormone" theory of the corticoids; Dustin's observations on the "caryoclastic poisons," the "post-operative disease," the curative action of fever, foreign proteins, and of other "non-specific therapeutic agents"; the "nephrotoxic sera" of Masugi; and to the "Goldblatt clamp" for the production of experimental renal hypertension.

At first sight it would seem that all these observations have little in common and that there is no reason to attempt their integration into a unified system of physiological and pathological events. Yet most of my research work has been devoted to the construction of bridges between these and many additional facts, since they were thought to be interconnected in nature. Through the comprehension of their unity we hoped to learn how to use them better for the understanding of life and the treatment of disease.

The keynote of this unification was the tenet that all living organisms can respond to stress as such, and that in this respect the basic reaction pattern is always the same, irrespective of the agent used to produce stress. We called this response the general adaptation syndrome, and its derailments the diseases of adaptation.

Anything that causes stress endangers life, unless it is met by adequate adaptive responses; conversely, anything that endangers life causes stress and adaptive responses. Adaptability and resistance to stress are fundamental prerequisites for life, and every vital organ and function participates in them. In order to present a well-proportioned outline of the general adaptation syndrome it was necessary, therefore, to peruse every branch of physiology, biochemistry, pathological anatomy, and clinical medicine in search of the "stress factor" in all aspects of normal and abnormal life.

It will take many years, indeed many generations, before the details of the general adaptation syndrome are satisfactorily elucidated. In fact, we shall never truly "understand" this phenomenon, since the complete comprehension of life is beyond the limits of the human mind. But there are many degrees of "elucidation." It seems that the fog has now been just sufficiently dispersed to perceive the general adaptation syndrome through that measure of "twilight" which permits us to discern the grandeur of its outlines but fills us with the insatiable desire to see more.

We realize that many lines in our sketch will have to be hesitant, some even incorrect, if we try to put on paper now what we still see only vaguely. But a preliminary map—albeit largely incomplete and partly inaccurate—is needed *now* by those eager to exploit this field which holds so much promise for all who suffer from stress. I hope that these pioneers in uncharted territories will accept my partial and distorted map in the spirit in which it is offered, to complete and rectify it.

It is in this sense that I should like the reader to consider the following synopsis of what I think I see.

Principal Facts and Theories upon which the General Adaptation Syndrome Concept is Based

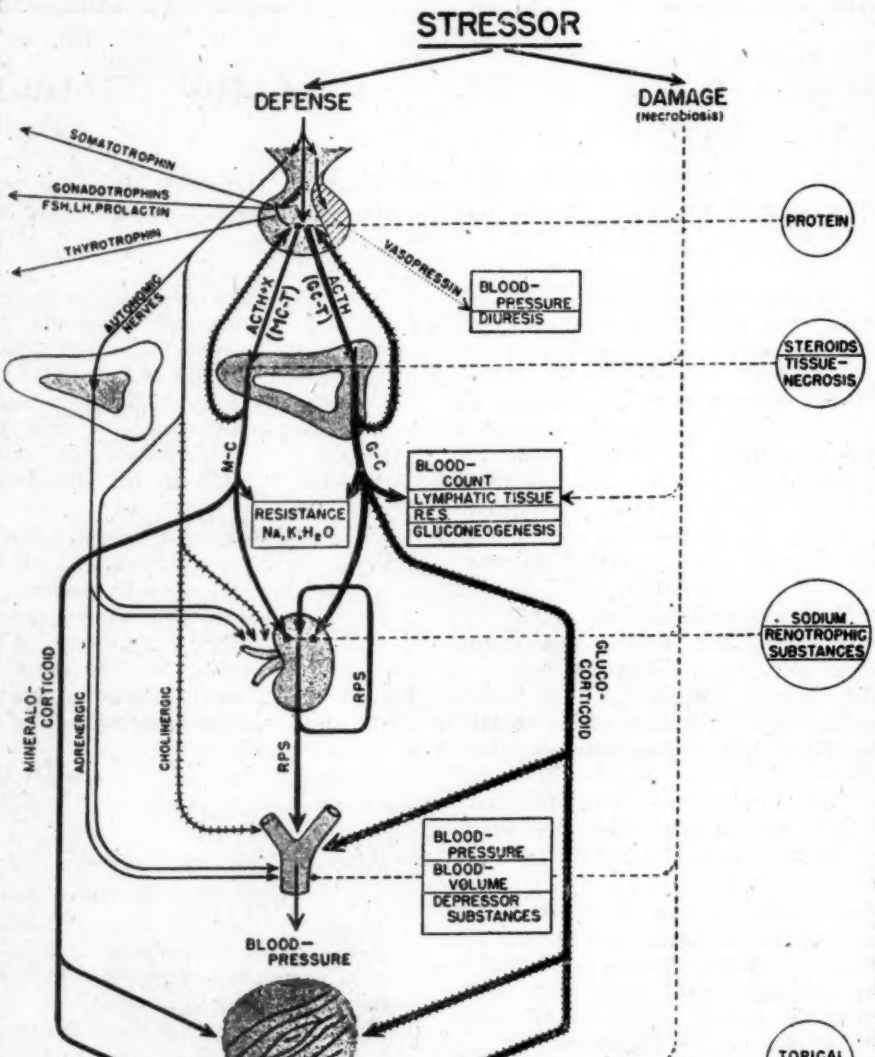
Apart from the many specific defence reactions (e.g., formation of specific antibodies, adaptation to cold, habituation to morphine, hypertrophy of much-used muscle groups) there is an integrated syndrome of closely interrelated adaptive reactions to non-specific stress itself; this has been termed the "General Adaptation Syndrome" (G.A.S.). It develops in three stages: the "Alarm Reaction" (A.R.), the Stage of Resistance, and the Stage of Exhaustion. Most of the characteristic manifestations of the A.R. (tissue catabolism, hypoglycaemia, gastro-intestinal erosions, discharge of secretory granules from the adrenal cortex, haemoconcentration, etc.) disappear or are actually reversed during the stage of resistance, but reappear in the stage of exhaustion. This suggests that the ability of living organisms to adapt themselves to changes in their surroundings, their adaptability or "adaptation energy," is a finite quantity; its magnitude appears to depend largely upon genetic factors.

In the general adaptation syndrome the manifestations of passive non-specific damage are intricately intermixed with those of active defence. This is an inherent characteristic of the stress which elicits the general adaptation

*The first part of the Heberden Oration, given on June 2, 1950. The second part, being principally a commentary on lantern slides, was summarized in the *British Medical Journal* of June 10.

syndrome. In the biological sense stress is the interaction between damage and defence, just as in physics tension or pressure represents the interplay between a force and the resistance offered to it.

In addition to damage and defence, every stressor also produces certain specific actions (e.g., anaesthetics act upon the nervous system, diuretics upon water metabolism, insulin upon the blood sugar) quite apart from their stressor effects. Hence the general adaptation syndrome never occurs in its pure form, but is always complicated by superimposed specific actions of the eliciting stressors. In contemplating any biologic response (e.g., a spontaneous disease, an intoxication, a psychosomatic reaction), it is usually quite difficult to identify individual manifestations as being due respectively to damage, defence, or specific actions of the provocative agent. Only non-specific damage and defence are integral parts of the general adaptation syndrome, but the specific actions of the eliciting stressors modify the course of the resulting general adaptation syndrome (e.g., the glycaemic curve will deviate from the characteristic pattern if insulin is used as the stressor agent; the neurological manifestations will be atypical if the general adaptation syndrome is provoked by ether). In this sense they act as "conditioning factors." Certain circumstances, not directly related to the stress situation, are also prone to alter the course of the general adaptation syndrome. Among these heredity, pre-existent disease of certain organ systems, and the diet are especially important.



The accompanying schematic drawing disregards the specific actions of stressors, since they are not part of the general adaptation syndrome. It attempts to depict only the main pathways through which non-specific stress itself affects the organism and the manner in which such reactions are conditioned.

Defence

The systemic defence measures, against both general and localized (topical) injuries, are co-ordinated through the hypothalamic vegetative centres and the hypophysis. The initial pathways through which stressors act upon these centres are not yet known. Probably either humoral or nervous impulses, coming from the site of direct injury, can induce the hypothalamus–hypophysis system to gear the body for defence. Subsequently both of the two great integrating mechanisms, the nervous and the endocrine system, are alerted.

The Nervous Defence Mechanism.—Nervous impulses descend from the hypothalamic vegetative centres, through the autonomic nerves, to the peripheral organs. The splanchnics induce the adrenal medulla to discharge adrenergic hormones (adrenaline and *nor*-adrenaline) into the blood. Other adrenergic nerves influence their target organs directly through fibres which in the final analysis again act through the liberation of adrenergic compounds, in this case at their endings in the effector organs themselves (blood vessels, glands, etc.). Presumably the discharge of adrenergic hormones into the circulation is most effective when they are needed throughout the body, while the sympathetic nerves are better suited to impart similar impulses selectively to certain circumscribed territories. The most conspicuous results of such neuro-humoral discharges are changes in the contractility of smooth muscle. Owing to an adrenergic vasoconstriction, peripheral resistance increases and the blood pressure rises. This hypertensive response may be further accentuated by an increased cardiac volume and the opening of the "renal shunt," which deviates blood from the cortical glomeruli to the juxtamedullary region of the kidney. This neurogenic activation of the "shunt" is quite comparable to that induced by mechanical interference with the arterial inflow (Goldblatt clamp, "endocrine kidney" operation) into the kidney; hence it augments the production of renal pressor substances (R.P.S.). The latter also cause peripheral vasoconstriction; thus they further augment peripheral resistance in the cardiovascular system and hence the blood pressure rises (cf. below).

There is some evidence of a simultaneous cholinergic discharge during systemic stress. Concurrent activation of both agonists and antagonists occurs in many effector systems during the general adaptation syndrome. Presumably it helps to stabilize the target organs in the face of very powerful stimuli which might otherwise cause excessive deviations from the norm. This concurrent tension of agonists and antagonists is somewhat reminiscent of the simultaneous contraction of flexor and extensor muscles —for instance in a limb—to prepare it against possible displacement by a blow which may come from any direction. However, damage (shock) endangers life particularly through vasodepressor and hypotensive actions; hence the predominant response during the general adaptation syndrome is a defensive (prophylactic) vasoconstriction and hypertension.

The nervous system also participates in many other defensive reactions during the general adaptation syndrome, e.g., the regulation of water metabolism (through the hypophysial stalk and posterior lobe), the blood sugar (through the hepatic branches of the sympathetic division), and the blood count (through splenic contraction), but for the sake of simplicity these are not specifically indicated in our schematic drawing.

Hormonal Defence Mechanism

The principal endocrine response to stress is characterized by the so-called "shift in anterior-lobe hormone production." This consists in a diminished secretion of somatotrophin, the gonadotrophins (F.S.H., L.H., prolactin) and thyrotrophin—which are not essential for the maintenance of life during conditions of emergency—accompanied by an increase in the secretion of A.C.T.H. Apparently the anterior lobe is unable to produce all its hormones at an optimal rate if it is called upon to discharge extraordinarily large amounts of corticotrophin.

A.C.T.H. is a "gluco-corticotrophic" hormone. It induces the adrenal cortex to produce predominantly gluco-corticoids—e.g., "compound F," cortisone. The latter act upon the blood count (lymphopenia, eosinopenia, polymorphonuclear leucocytosis), the thymico-lymphatic tissue (lympholysis), the reticulo-endothelial system (increased phagocytosis and antibody formation), and gluconeogenesis (transformation of non-sugars into carbohydrates).

The gluco-corticoids presumably influence resistance in many additional ways which have not yet been fully analysed. Through all these actions such steroids help to maintain adrenalectomized animals, even during exposure to stress.

All gluco-corticoids so far examined possess some mineralo-corticoid activity (actions upon Na, Cl, K, and water metabolism); thus they resemble the pure mineralo-corticoids, but the latter are much more potent in this respect and possess no gluco-corticoid action. Hence, changes in mineral and water metabolism observed after the injection of A.C.T.H. do not necessarily reflect the production of pure mineralo-corticoids by the adrenal.

The action of gluco-corticoids upon the kidney has not yet been extensively studied. However, preliminary investigations show that they cause marked hyperaemia of the glomeruli and may render the latter permeable to proteins and even blood. Heavy overdosage with gluco-corticoids can produce severe hyalinization and disintegration of glomeruli This is followed by a rise in blood pressure, presumably mediated through the R.P.S. system. In this respect gluco-corticoids and mineralo-corticoids may mutually synergize each other.

The gluco-corticoids inhibit the production of arteriosclerotic changes (especially periarteritis and hyalinosis). In this respect they antagonize the effects of mineralo-corticoids.

The gluco-corticoids generally inhibit excessive proliferation of fibrous tissue, the formation of intercellular protein deposits (e.g., hyalinosis, collagen disease, allergies) and excessive granulomatous defence reactions against those local irritants which stimulate fibroplastic inflammatory reactions in mesenchymal tissue. They also tend to decrease the erythrocyte sedimentation rate (E.S.R.) through their effect upon the blood proteins. In all these respects they act as antagonists of the mineralo-corticoids.

The mechanism of the marked anti-allergic and anti-histaminergic actions of gluco-corticoids has not yet been elucidated It may depend upon the breakdown of the proteins which store histamine as a protein–histamine complex.

Many data suggest that under conditions of stress mineralo-corticoid production is likewise increased. Such a rise can also be elicited by certain impure, mineralo-corticotrophic, anterior-pituitary extracts—for instance, lyophilized anterior-pituitary tissue (L.A.P.). Threshold doses of L.A.P. are further activated in this respect by simultaneous administration of A.C.T.H. Apparently the action of the latter can be qualitatively altered by some factor ("X") present in crude pituitary extracts and L.A.P. This "X factor" appears to be a specific pituitary principle, as it has not been found to occur in similar preparations of other tissues (e.g., liver). The "X factor" is manifestly not A.C.T.H., but it may be identical with one of the other, already known, hypophysial hormones. It could also be a special hypophysial principle, not hitherto identified. Be this as it may, it has now definitely been established that certain pituitary extracts produce a gluco-corticoid type, others a mineralo-corticoid type of reaction. Furthermore, in response to stress the pituitary itself may discharge predominantly gluco-corticotrophic or mineralo-corticotrophic principles.

Mineralo-corticoids

The mineralo-corticoids share with the gluco-corticoids the ability to increase the general resistance of adrenalectomized animals. They also cause severe lesions in the kidney, if large quantities of them are given over a long time. There is distension of the convoluted tubules, proliferation of the spiral segments, hyalinization of the glomeruli, proteinuria, hyaline-cast formation, and, eventually, nephrosclerosis.

It is highly probable that mineralo-corticoids increase the production of renal pressor substances, especially through some direct functional effect upon the convoluted tubules. Even the subsequent morphological changes in this part of the nephron precede the development of glomerular sclerosis. Eventually, however, the gradual constriction of the glomerular capillary bed acts somewhat like the Goldblatt clamp or the "endocrine kidney" operation and, simultaneously with the inhibition of glomerular filtration, increases the endocrine activity of the nephron. At the same time the inactivation of renal pressor substances is impeded and a hormonally induced renal hypertension ensues.

Presumably, both stimulation of R.P.S. formation and inhibition of R.P.S. destruction is thus induced by mineralo-

corticoids. This affects the blood vessels. At first the resulting excess of renal pressor substances causes a functional vasoconstriction with an increase in peripheral resistance and blood pressure. More prolonged overdosage with mineralo-corticoids results in arteriosclerotic changes (especially periarteritis nodosa and hyalinosis), with a consequent permanent increase in peripheral resistance and blood pressure.

In this respect mineralo-corticoids and gluco-corticoids mutually antagonize each other, but since (at least at certain dose levels) their actions upon the kidney are synergistic, it depends upon the "conditioning" circumstances whether the administration of gluco-corticoids to animals overdosed with mineralo-corticoids increases or decreases the blood pressure. (Cf. also conditioning effect of sodium and renotrophic substances, below.)

There is no definite evidence to prove that either type of corticoid has any direct vasopressor effect. Addition of corticoids to perfused vessel preparations does not cause them to contract. Nevertheless, mineralo-corticoids can augment the blood pressure even in the absence of the kidney, presumably by raising the blood volume through their effect on mineral and water metabolism.

Both types of corticoids act back upon the anterior lobe and inhibit its A.C.T.H. production through the so-called phenomenon of "compensatory atrophy." It is not yet known whether corticoids also impede the endogenous production of that "X factor" which renders A.C.T.H. mineralo-corticotrophic. However, this is very probable, since otherwise A.C.T.H. therapy would only aggravate conditions characterized by symptoms of mineralo-corticoid overdosage. If the production of the "X factor" is inhibited in the same manner as that of ordinary A.C.T.H., then the therapeutic action of A.C.T.H. is readily explicable. In both instances the pituitary is exposed to an excess of gluco-corticoids. The latter are even more potent in eliciting the "compensatory atrophy" phenomenon than the mineralo-corticoids. Consequently, endogenous corticotrophic stimuli (including "X factor") are virtually eliminated and the exogenously administered, predominantly gluco-corticotrophic A.C.T.H. acts uninfluenced upon the adrenal cortex.

There is much to suggest that at least certain types of stress (e.g., emotional stimuli) can increase the production of antidiuretic hormone, which is probably identical with vasopressin. This effect is undoubtedly mediated by nerve tracts descending from the hypothalamus to the posterior lobe, since (unlike the discharge of A.C.T.H.) it is abolished by transection of the hypophysial stalk.

Vasopressin exerts important effects upon the blood pressure and diuresis; these may be superimposed upon the typical reaction pattern during the general adaptation syndrome. However, the role of vasopressin secretion during systemic stress has not yet been adequately investigated.

Damage and Other Factors Conditioning Defence

As we have said before, many non-specific actions of stressors merely represent manifestations of damage and are not mediated through either the humoral or the nervous defence systems outlined above. These changes appear to result from necrobiosis of cells not sufficiently protected by the systemic defence mechanism. Thus tissue catabolism occurs under conditions of stress even in the absence of the pituitary, the adrenals, or the sympathetic nervous system. Although gluco-corticoids enhance catabolism, especially of readily dispensable proteins (e.g., that of the thymus, the lymph nodes, and connective tissue), extensive losses of body protein, fat, and carbohydrate can occur even after adrenalectomy.

Catabolites thus produced can condition the defensive chain-reaction of the general adaptation syndrome at various links. We have seen that protein tends to favour the mineralo-corticotrophic type of hypophysial discharge; that sodium increases, while renotrophic steroids decrease, the sensitivity of the kidney to overdoses of mineralo-corticoids, that topical chemical irritation augments the fibroplastic- and hyalinosis-producing action of mineralo-corticoids, and so forth. There is every reason to believe that endogenously liberated protein (or amino-acids), sodium, renotrophic steroids, and irritating metabolites would influence such hormone actions in the same manner as these substances do when they are exogenously introduced into the body. The intensity and the quality of such "endogenous self-conditioning" of the general adaptation syndrome largely depend upon the body's reserve of these metabolites and the intensity with which they are discharged into the blood. Presumably this in turn is influenced by heredity, species differences, previous exposure to stress, the nutritional state of the organism, etc.

We saw that the specific actions of individual stressors may likewise act as conditioning factors. Thus agents causing intense renal damage can sensitize the body to the pressor effects of the general adaptation syndrome, somewhat in the same manner as partial nephrectomy does; pyrogens, histamine, and other stressors capable of causing severe vascular paralysis will selectively "decondition" the arterial tree to the pressor action of endogenous renal pressor substances; microbes, allergens, or local mechanical trauma can stimulate the tissues which come into direct contact with them (somewhat like the formalin or mustard in our "topical irritation arthritis" test) to the formation of a fibroplastic and hyalin-containing granuloma tissue.

Such conditioning factors affect the defence mechanism at different points and may either increase or decrease the efficacy of any one among its individual components. Hence it is evident that the essentially stereotyped defence-pattern of the general adaptation syndrome can manifest itself in widely different ways, depending upon such conditioning factors.

Diseases of Adaptation

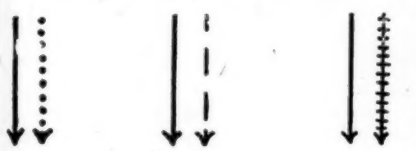
This is particularly important for the understanding of the diseases of adaptation. Unless conditioning factors could considerably alter the reaction-pattern to stress, it would be impossible to ascribe rheumatoid arthritis, periarteritis nodosa, allergies, certain types of diabetes, or hypertension to the same causative agent—namely, to systemic stress. The concept that such widely different maladies should result from the same cause has often been considered to be quite contrary to accepted views concerning the causation of disease. Since this tenet is rather fundamental for our interpretation of the diseases of adaptation, it deserves special attention.

Let us point out first that such an assumption is not without precedent in medicine. For example, excessive production of thyroid hormone may be associated with predominantly ophthalmic, metabolic, or cardiac derangements. Before the tubercle bacillus had been isolated it would have been considered most improbable that such dissimilar conditions as Pott's disease, phthisis of the lungs, miliary tuberculosis, and tuberculous lupus of the skin were all caused by the same pathogen; yet this is the case.

We have attempted to demonstrate that the polymorphism of the general adaptation syndrome symptomatology is due to two principal reasons. First, every stressor has specific actions, in addition to its stress-producing ability. The former modify the response caused by stress as such; hence the polymorphism of the general adaptation syndrome manifestations can be due to specific effects of the evocative stressors.

The following schema will illustrate this point. In all three figures the solid arrow represents stress, the other the "contaminating" specific actions. Obviously, the end results of exposure to the three agents represented here could not be the same.

This type of "conditioning" may also be illustrated by an example taken from chemistry. All acids have many properties in common, yet the reactions of each member in this group are essentially different. The characteristics which they share are due to their acidity; the properties which distinguish them are the specific reactions of the carriers of this acid function. In pharmacology the stressor effect is what the drugs have in common; their other properties endow them with "specific pharmacological actions." Both in chemistry and in pharmacology the specific properties condition that non-specific feature (acidity, stress) which the entire group shares. Hence no two acids—and no two stressors—act exactly alike. This may help to illustrate conditioning by specific properties of the stressor.



We have seen, however, that even exposure to the same stressor agent may result in qualitatively different responses. Here polymorphism of the general adaptation syndrome manifestations is due to selective conditioning by factors extraneous to the stressor. This "peripheral conditioning" may occur at the various intermediate stations of the general adaptation syndrome or in the target organs themselves. We have compared this to the manifold effects one can obtain with the same electric current. During an emergency it may be necessary to supply more electricity for a community. This current will always be of the same quality and it will always travel along the same pre-existent main channels. Yet, depending upon the kind of emergency and the special needs of each district, both its quality and its quantity have to be regulated locally in the periphery. Thus the same current can be used to produce mechanical work, sound, light of any colour, heat, or cold, and indeed it may be shut out completely from a locality where it would represent a fire hazard. Of course, the more we approach the periphery of such an electric circuit the more subject it will be to conditioning. First, because the thin terminal wires can more easily be handled than the thick principal cables, and, secondly, because interventions anywhere along the line, above such a peripheral point, would affect the latter.

Essentially the same is true of the general adaptation syndrome. The more we approach the periphery the more often do we note deviations from the standard general adaptation syndrome pattern. All stressors cause an A.C.T.H. discharge, but this may or may not be accompanied by the production of the "X factor," which is necessary for mineralo-corticotrophic actions. Interference at a lower level may cause even more selective deviations from the typical stress response. Thus, transection of the splanchnics may impede adrenaline discharge during the alarm reaction without interfering with any general adaptation syndrome manifestations except those resulting directly from hyperadrenalinaemia. Possibilities for conditioning become ever more selective as we approach the peripheral target organs, each of which can be individually protected or sensitized to the typical actions of the general adaptation syndrome.

It is an inherent characteristic of most ramifying systems that side branches are more readily influenced than main lines. The following schematic drawing will help to illustrate this.

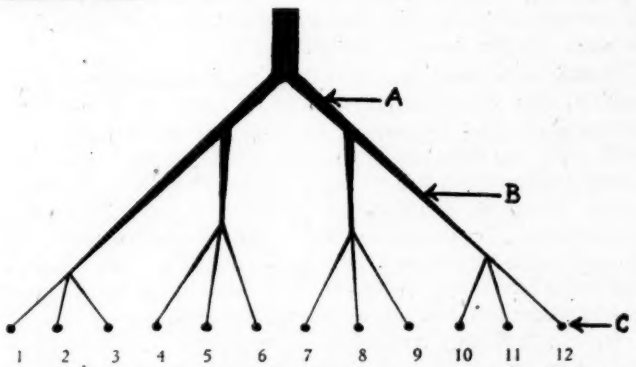


Illustration of selective conditioning in a ramifying system. Here 12 target organs received impulses through branches of a single main line. Conditioning at A would affect targets 7–12 without affecting targets 1–6. Conditioning at B permits targets 10–12 to be singled out specifically. Conditioning at C influences only the one target organ marked 12.

Principal Criticisms of the General Adaptation Syndrome Concept

The general outlines of the general adaptation syndrome concept have not been challenged, but some of its aspects became the subject of much debate and criticism; these deserve special consideration here.

Why are the "Diseases of Adaptation" so Polymorph in their Manifestations if they are all due to Stress?—We mention this question only for the sake of completeness, since it has already been answered in the preceding section. We believe that the principal reasons for this polymorphism are the so-called "conditioning factors"; namely, the specific effects of the evocative stressors and other exogenous or endogenous factors (heredity, pre-existent disease of certain organs, diet, previous exposure to stress, etc.) which can effect, selectively, certain pathways or target organs of the general adaptation syndrome response.

Why does Exposure to the same Stressor produce Disease only in certain Individuals?—It is undoubtedly true that the same drug, microbe, emotional irritant, or physical injury may produce a disease of adaptation in one person and be tolerated with impunity by another. It should be recalled, however, that the general adaptation syndrome is a useful, normal physiological reaction to stress; only its derailments have been interpreted as diseases of adaptation. Hence exposure to a stressor can be expected to produce such diseases only if the defence reaction is inadequate. Thus, for instance, in our experimental efforts to produce the hyalinosis–hypertension syndrome in rats by exposure to cold we found it necessary to perform unilateral nephrectomies and to keep the animals on high-sodium, high-protein diets. All these conditioning circumstances failed to produce disease in the absence of stress, but upon exposure to cold they caused a derailment of the general adaptation syndrome, with consequent cardiovascular lesions, nephrosclerosis, and a rise in blood

pressure. It is very probable that in man also, under the influence of stress, similar diseases would develop only when the general adaptation syndrome is prevented from evolving in a normal manner, as a result of adverse conditioning factors.

Desoxycorticosterone (D.C.A.) may not Occur in the Adrenals.—The fundamental work concerning the diseases of adaptation has been performed in animals treated with excesses of D.C.A. It is this work which led to the concept that diseases could be due to an excessive mineralo-corticoid production. Yet evidence now at hand is insufficient to prove with certainty that desoxycorticosterone is produced, as such, by the adrenal cortex.

It will be recalled that L.A.P. (a mineralo-corticotrophic extract) also causes similar lesions in intact though not in adrenalectomized animals. Even if desoxycorticosterone itself were not secreted by the suprarenal cortex, the above observations would still strongly suggest that some similarly acting principle is produced as a result of hypophysial stimulation. Furthermore, the "amorphous fraction" of Kendall, the "sodium factor" of Hartman, and desoxocortisone have all been shown to possess typical mineralocorticoid actions. All these substances have been prepared from the adrenals by several investigators and in good yields, so that there can be no question about their being natural products of suprarenal activity.

The Doses of D.C.A. used in the Fundamental Experiments on the "Diseases of Adaptation" may exceed the Amounts produced endogenously by the Adrenal itself.—This criticism has been voiced particularly with regard to the earliest experiments, in which D.C.A. was given in the form of injections to non-sensitized animals. Subsequently, with the introduction of the pellet implantation technique, especially in animals sensitized by unilateral nephrectomy and/or high-sodium diets, much smaller amounts of the hormone proved to be disease-producing.

It must be remembered, furthermore, that there is no objective reason to consider the pathogenic amounts of mineralo-corticoids as being beyond the limits of what could be produced in the body during stress. The quantities excreted in the urine of men who had received D.C.A. in doses conducive to hypertension, increased blood volume, oedema, and renal damage do not exceed those eliminated by patients after burns, traumatic injuries, or acute infections. If we can judge by the amounts of glucocorticoids required to produce remissions in those spontaneous diseases which have been simulated in the animal by D.C.A. overdosage, then this criticism appears to be even more unjustified. About 10 mg. of D.C.A. a day, given over a period of weeks, would certainly be pathogenic in man, while 80–100 mg. of cortisone is usually required to produce a pronounced remission, for instance, in rheumatoid arthritis or lupus erythematosus.

How can one Reconcile the Fact that the "Rheumatic-allergic type" of Disease is produced by Corticoids in Animals and nevertheless responds so favourably to Corticoid Therapy in Man?—This question hardly deserves much comment now, although it was often asked just after the introduction of cortisone into clinical practice. The original animal experiments of necessity had to be performed with D.C.A. (a mineralo-corticoid), since this was the only adrenal steroid available in adequate amounts. Its effects upon many target organs are the reverse of those produced by gluco-corticoids (e.g., cortisone). As we now know, this is due partly to a peripheral antagonism at the level of the target organs themselves and partly, perhaps, also to the inhibition by gluco-corticoids of mineralocorticoid production, through the "compensatory atrophy" phenomenon.

The Urinary Elimination of Corticoids is not always demonstrably Abnormal in the Diseases of Adaptation.—As we have repeatedly emphasized in this paper, diseases of adaptation do not necessarily result from an absolute deficiency or excess of corticoids; they can also ensue as a consequence of an improper balance between gluco- and mineralo-corticoid secretion, or be caused by a state of "relative hypocorticoidism." Thus in our "topical irritation arthritis" the introduction of an irritant into the joint region produced a violent arthritis in perfectly normal animals, yet it failed to do so after pre-treatment with an excess of A.C.T.H. or cortisone. This clearly shows that the adequacy of corticoid production can be assessed only in proportion to the pathogen which creates a need for such hormones. It is highly probable that pathogenic factors which cause disease in individuals whose corticoid production remains "normal" would fail to do so if the adrenals responded with an increase in hormone discharge commensurate with the increased requirements occasioned by an abnormal situation. Indeed, it is quite possible that many individuals who carry the pathogens (whatever these may be) of rheumatoid arthritis, allergies, lupus erythematosus, and so forth can remain in perfect health throughout life because—through the general adaptation syndrome mechanism—they have rendered these potential pathogens quite innocuous. To use an analogy from an entirely different field, one might compare them with the typhoid or meningococcus carrier who lives in perfect harmony with the deadly germs present in his body.

It should be mentioned, furthermore, that some evidence of an anomaly in steroid metabolism has been noted in patients suffering from the rheumatic–allergic diseases (e.g., increased pregnandiol excretion after the administration of progesterone, anomalies in 17-ketosteroid elimination).

Research along these lines has been handicapped, principally because of the difficulty of assaying blood or urine specifically for mineralo-corticoid activity. However, several recently published improvements in the relevant techniques hold great promise as regards the elucidation of this important problem.

Clinical Applications of the General Adaptation Syndrome Concept

As regards clinical medicine, we feel that the principal value of the general adaptation syndrome concept is that, by helping us to understand the role of the stress factor in disease, it enables us to adjust our therapeutic measures accordingly.

Non-specific Therapy.—It becomes increasingly more evident that many of the time-honoured, though not spectacularly effective, non-specific therapeutic measures—such as fever therapy, shock therapy, parenteral administration of foreign proteins, blood-letting, or mere starvation—are beneficial, largely through the general adaptation syndrome. Often their principal value appears to be that they stimulate A.C.T.H. and gluco-corticoid production. Wherever this is so, it may be preferable in the future to inject A.C.T.H. or cortisone. In certain instances, however, non-specific therapy proved efficacious where A.C.T.H. failed. For instance, in mental patients who did not respond to A.C.T.H. it could be shown by subsequent shock therapy that they are benefited by non-specific stress. Here presumably certain specific changes, incident to the shock, act as conditioning factors of the hypophysis–adrenal

discharge, or separately through other channels of the general adaptation syndrome (e.g., the nervous system or the catabolic response of the alarm reaction).

There is a striking parallelism between the diseases empirically shown to respond to non-specific therapy and those which show dramatic remissions under the influence of A.C.T.H. and cortisone (e.g., rheumatoid arthritis, various inflammatory conditions of the eye, allergies). Through the use of the corticotrophic and corticoid hormones we are on the threshold of developing a modern version of non-specific therapy which is much more effective than the old and lends itself better to a scientific analysis of its mechanism.

Dietary Treatment of Cardiovascular and Renal Diseases.—Diets poor in seasoning (spices, salt) and/or protein have long been recommended in the treatment of hypertension, nephritis, nephrosis, and allied conditions. However, the results were rarely spectacular, and, in the absence of any convincing rationale which could justify their use, they have not been received with sustained enthusiasm. Purely empirical observations on a heterogeneous clinical material failed to show clearly even whether the detrimental effects of highly seasoned food are due to sodium, chloride, or condiments in general. It also remained a subject of debate whether certain vegetable proteins are more readily tolerated than meat, and especially whether—in the face of heavy urinary protein losses in renal disease—it is better to prescribe low-protein diets, to protect the kidney against overwork, or rations rich in protein, to substitute for the constant urinary losses.

A study of the mechanism through which stress causes cardiovascular and renal disease has established certain definite facts concerning the part played by protein and minerals in the pathogenesis of the experimental replicas of such maladies. If these data can be applied to the corresponding clinical diseases—and there is much reason to think that they can—then we shall soon be able to prescribe diets on a much more rational basis.

Corticotrophin and Corticoid Therapy.—Undoubtedly the most important pertinent data are those derived from the clinical use of A.C.T.H. and cortisone. Since only very limited amounts of these hormones have been available up to date, it is not yet possible to assess their scope accurately. However, it is precisely now that some general orientation in this field is most urgently needed. By way of a summary, let us say, therefore, that (apart from their obvious utility in hypocorticoidism and anterior-pituitary deficiency) A.C.T.H. and/or cortisone have been shown to be of value in the following conditions:

Agranulocytosis
Alcoholism
Allergies, various (in addition to those specifically mentioned here)
Allergic rhinitis
Asthma
Atopic dermatitis
Blepharitis
Choroideremia
Choroiditis
Conjunctivitis vernalis
Dermatomyositis
Drug sensitization
Eczema
Exfoliative dermatitis
Erythema multiforme
Fevers (apparently irrespective of aetiology, though probably normalization of the temperature is not always an advantage)
Gouty arthritis
Hay-fever
Haemolytic anaemias of various kinds
Herpes zoster
Hodgkin's disease
Idiopathic hypoglycaemia
Iritis
Iridocyclitis
Keratitis
Leukaemias (various)
Loeffler's syndrome
Lupus erythematosus disseminatus
Lymphosarcoma
Nasal polyps
Nephrosis
Neurodermatitis
Ophthalmologic conditions (especially those characterized by allergic and inflammatory manifestations)
Periarteritis nodosa
Pneumonia (pneumococcus, "primary atypical")
Psoriasis
Retinitis (centralis, pigmentosa)
Retrobulbar neuritis
Rheumatic fever
Rheumatoid arthritis and spondylitis
Serum sickness
Tuberculosis of the larynx
Ulcerative colitis
Urticarias (various)
Uveitis
Vasomotor rhinitis

Preliminary data suggest that this type of treatment may also be of value in the following conditions:

Boeck's sarcoid
Glaucoma
Hepatitis
Hypertension
Hyperthyroidism (especially in normalizing the B.M.R. and reducing the exophthalmos)
Keloids
Liver cirrhosis
Myasthenia gravis
Nephritis (especially if due to allergy)
Pemphigus
Scleroderma
Thromboangiitis obliterans (Buerger)

Available data suggest that A.C.T.H. and/or cortisone are of no value in:

Amyotrophic lateral sclerosis
Carcinomas of most types
Congestive heart failure
Diabetes mellitus
Multiple myeloma
Poliomyelitis

A.C.T.H. and/or cortisone may produce harmful effects in:

Acne vulgaris
Congestive heart failure
Cushing's syndrome
Diabetes mellitus
Hypertensive disease of certain types
Nephritis of certain types
Osteoporosis
Peritonitis
Septicaemia
Wound healing

In this connexion it should also be emphasized that under certain conditions A.C.T.H. and/or cortisone may actually cause:

Acute pulmonary oedema
Ascites
Marked decrease in resistance to infections
Obscuring of the criteria of disease (e.g., fever and abdominal rigidity in peritonitis, the haematological manifestations of systemic diseases, the acceleration of the pulse in acute infections, etc.)

Problems for Future Research Concerning the General Adaptation Syndrome

At this point it may be stimulating to contemplate some of the most important tasks that lie before us. However, in order to do so effectively we must first consider the direction this type of work has taken during the last few years.

In 1947 I emphasized that: "For the species, the most important role of the hormones is reproduction, but for the individual it is differentiation and adaptation. It becomes increasingly more obvious, furthermore, that the principal medical application of endocrinology is not the treatment of the primary but of the secondary diseases of the endocrines. Tumours and hyperplasias of endocrine glands, with consequent hormone overdosage, or destruction of incretory organs with the resulting hormone deficiency syndromes, are instructive simple experiments of nature which have taught us much about the endocrines. But these are rare diseases in comparison with the hormonal derangements resulting from maladaptation to stress.

"The main fatal syndromes of internal medicine (various cardiovascular, renal rheumatic, and old-age diseases) may belong to this latter group; they are probably by-products of faulty hormonal adaptative reactions to a variety of non-hormonal pathogenic agents. The apparent cause of illness is often an infection, an intoxication, nervous exhaustion, or merely old age, but actually a breakdown of

the hormonal adaptation mechanism appears to be the most common ultimate cause of death in man" (Selye, 1947).

Similar considerations led Albright (1943) to point out that: "The physician who calls himself an endocrinologist and confines his interests to such unfortunate members of society as might appear in the side-show of a circus never realizes that pneumonia, a broken leg, and a bad burn involve important changes in adrenal cortical function (cf. 'alarm reaction' of Selye), that the disturbance in homoeostasis occasioned by chronic renal insufficiency is ameliorated by a secondary hyperparathyroidism, that the somatotrophic action of testosterone propionate may be of use in many conditions other than male hypogonadism, and so on."

Laroche (1948) stressed particularly in connexion with the experimental work on the general adaptation syndrome that: "These experiments throw a new light upon a series of maladies which could not hitherto be related by pathologists to any particular hormonal derangement: certain hypertensions, certain types of chronic nephritis, the rheumatic affections, periarteritis nodosa, etc. Since these conditions can be elicited by a hormonal derangement, one wonders whether it would not be possible to effect their re-equilibration by means of other hormonal actions?"

I pointed out that: "It would be tempting to survey all the diseases of unknown aetiology from this new point of view and to determine whether those among them which apparently can be caused by a variety of agents belong to the category of the diseases of adaptation" (Selye, 1946). This has been accomplished, to the best of my ability, in my book now about to be published. Let us consider now some of those questions the solution of which appears to be particularly rewarding when we survey the general adaptation syndrome concept as it presents itself during the early months of 1950.

Adaptation Energy.—Ever since 1937 I have been intrigued by the fact that an already acquired adaptation to a certain stressor agent is gradually lost in the course of chronic exposure. This means that the "adaptation energy" (or adaptability) of the organism is a finite amount. There is a singular similarity between the manifestations of the exhaustion stage, which ensues when adaptability is lost, and those of physiological senility. No doubt inestimable advantages would accrue to the practice of medicine if we succeeded in identifying "adaptation energy." So far we can report no progress along these lines.

The Physio-pathology of Periodicity.—In addition to the irreversible exhaustion of senility, or of the "exhaustion stage" in the general adaptation syndrome, there is a temporary exhaustion or fatigue which ensues after less prolonged exposure to stress. From this condition recovery occurs most readily as a result of rest.

Stress-reactions—such as the general adaptation syndrome—are optimally effective during short emergencies; perhaps largely because most of the "stress hormones" (adrenergic substances, A.C.T.H., corticoids, R.P.S.) are well tolerated only during short periods and tend to cause severe complications if they act upon the body persistently over a long time. Thus, for example, the amounts of endogenous corticoids which spill over into the urine during a brief emergency (e.g., burns, emotional upsets, trauma, muscular work) are as high as those found in Cushing's disease, yet they do not produce "Cushingoid" manifestations. The same is true of patients who receive large amounts of such hormones for medicinal purposes during a short time. The intermittent secretion of A.C.T.H. during various stress situations (infections, nervous stimuli, etc.) may also explain the comparative rarity of "Cushingoid" changes in chronic disease; though here "deconditioning" metabolic changes probably also play a part. It may be rewarding to examine the mechanism of recovery from brief periods of overdosage with the "stress hormones" in order to learn how to avoid complications when they are therapeutically administered.

But there are many other data to stimulate interest in "periodicity."

A certain degree of cyclicity is nearly as characteristic of life as adaptability itself, and the lack of periodicity, or rigidity, is almost equivalent to death. The female sexual cycle, the pulse, the sleep rhythm with all the concomitant diurnal variations, the interchange between activity and rest, between work and play, the periodic renewal of cells in various organs are all indispensable for the maintenance of normal life. Stressors tend to disrupt this periodicity in many ways. It would be interesting to examine the possible relations between the diseases of adaptation due to stress and what might be called the "diseases of periodicity."

From time to time we feel the urge to reorganize our classifications in medicine, even if nothing really new is added—just as we rearrange the contents of our desk-drawers. It gives us a chance to eliminate the useless objects and to put the most useful ones into accessible positions. It may even call to our attention some long-forgotten item which we banished into obscurity at a time when we failed to realize its now so obvious utility.

We found it of interest to rearrange medicine in the book to which I referred above according to the general adaptation syndrome concept, but it may be equally, or even more, fruitful for some future investigator to rearrange them as "diseases of periodicity."

The Problem of the "First Mediator."—In the course of my work I have repeatedly had occasion to deplore the paucity of information concerning stimuli which, during stress, induce the pituitary to discharge A.C.T.H. Transection of the stalk (with all its nervous and blood-vessel connexions between hypophysis and hypothalamus) does not necessarily impede this response. The nervous pathways between the hypothalamus and the pituitary may be of importance in the event of exposure to purely neurogenic stressors; it remains to be seen, however, what carries the "stress message" to the anterior lobe from a burned skin, a traumatized limb, or tissues damaged by systemic infections and intoxications. I have expressed the opinion that perhaps an A.C.T.H. discharge could be caused by any derangement in the chemical or physical characteristics of the blood, but this is merely a hypothesis. Further work along this line is badly needed.

The possible Therapeutic Value of General Adaptation Syndrome Components, other than Adrenaline, A.C.T.H., and Gluco-corticoids.—Up to now attention was principally focused upon the utility of the adrenaline and gluco-corticoid discharges, the former mediated by the sympathetic, the latter by A.C.T.H. It is highly probable that many other manifestations of the general adaptation syndrome participate in raising resistance. In this connexion one might think of *nor*adrenaline, mineralo-corticoids, anti-diuretic hormone (vasopressin), acetylcholine, histamine, the products of lympholysis, and even endogenous anti-histamines.

How Perfect is the Correlation between Gluco-corticoid and Anti-arthritic Activity?—Up to the present time all our observations suggest that the power of a compound to inhibit rheumatoid arthritis or "topical irritation arthritis," to cause thymico-lymphatic involution, eosinopenia, and glycogen deposition in the liver and to antagonize certain manifestations of the "hyalinosis syndrome" are all correlated activities. In the terms of steroid pharmacology this would mean that these are subordinate actions of the gluco-corticoid potency, just as vaginal cornification, uterine oestrus, and testicular atrophy are subordinate actions of the folliculoid (oestrogenic) potency. It is not certain, however, that this apparent lawfulness will apply to all steroids which may become available in the future. There is some reason to believe that cortisonediene (a compound differing from cortisone by the introduction of a second double-bond at C_{6-7}) possesses certain gluco-corticoid activities without being capable of causing a remission in clinical rheumatoid arthritis. Further elucidation of these aspects of steroid pharmacology would undoubtedly extend the scope of pharmaco-therapy in the diseases of adaptation.

How Perfect is the Correlation between Mineralo-corticoid and Hyalinosis Activity?—In general, preparations with marked mineralo-corticoid actions (NaCl retention, K elimination, diuresis) are also most effective in producing experimental hyalinosis. However, in comparing the actions of L.A.P., desoxocortisone, and desoxycorticosterone this parallelism does not appear to be perfect. Furthermore, at very high dose levels, in certain vascular territories (e.g., kidney) even gluco-corticoids can cause hyalinosis, though in other target organs they inhibit such changes even at the same dose levels. We wish to stress the need for a more profound analysis of the correlation between mineralo-corticoid and hyalinosis activity.

Selective Conditioning in General.—We saw that some factors (diet, drugs, etc.) can selectively increase or decrease the action of stress hormones upon certain organs. In order to accentuate the desirable and to minimize the undesirable effects of A.C.T.H. and cortisone it is imperative to learn more about the activities of such "conditioning factors."

Selective Conditioning of the Adrenal Response in Particular.—The possibility of influencing the adrenal, at will, to produce different kinds of hormones deserves special mention. The adrenal cortex can produce a variety of compounds—namely, mineralo-corticoids, gluco-corticoids, testoids, folliculoids, and perhaps even "lipo-corticoids." We have shown, furthermore, that the morphological response of the adrenal cortex can also be qualitatively altered by conditioning factors. We concluded that the pharmacology of the adrenal cortex is not merely limited—as has hitherto been thought—to a more or less intense stimulation by A.C.T.H. It would be of the greatest interest to learn more about the factors which permit us to induce the adrenal cortex to respond in qualitatively different ways.

In this respect the recently discovered "X factor," which appears to be present in impure A.P.E. and L.A.P., is of special interest. It may be a new hormone or a mixture of already identified anterior-lobe principles. In any case, we shall have to attempt its identification in order to understand how the hypophysis can react to stress by discharging mineralo- and gluco-corticoids in variable proportions.

The recent demonstration that *nor*adrenaline is produced by the adrenal medulla raises the possibility of its participation in emergency reactions. Up to now only adrenaline has been considered in this connexion. Are there factors which can condition the adrenal medulla to produce either adrenaline or *nor*adrenaline predominantly?

Selective Hypocorticoidism.—The problem of selective hypocorticoidism is closely related to that previously discussed. The syndrome produced by excess mineralo-corticoids has often been compared to that of adrenal insufficiency. In both instances there is a tendency to develop hypoglycaemia, a predisposition to arthritis, a decreased resistance to various types of stressors, and, in certain circumstances, thymico-lymphatic hyperplasia. In these respects, manifestations of hypocorticoidism resemble those of a mineralo-corticoid excess. On the other hand, hypertension and hyalinosis are characteristic only of the latter. The relationship between complete hypocorticoidism (as caused by adrenalectomy) and selective hypo-gluco-corticoidism (as induced by mineralo-corticoid overdosage) requires further study.

Why is R.P.S. Maximally Produced When it is Minimally Detoxified?—It has been noted that conditions which cause the kidney to produce an excess of R.P.S. also interfere with its ability to detoxify such pressor substances. Indeed there appears to be a rather close inverse parallelism between R.P.S. production and R.P.S. detoxification. Perhaps such compounds as D.C.A. and such interventions as the "endocrine kidney" operation change the direction of a reversible chemical reaction between R.P.S. and some inactive precursor. If in the body the total amount of R.P.S. plus its precursor was fairly constant, factors which would tend to direct the process towards R.P.S. production would then automatically diminish its inactivation. This is but one of many possible explanations of the observed facts, but in view of the great practical importance of renal hypertension the field certainly deserves a systematic analysis.

Why is A.C.T.H. (or Cortisone) Capable of Producing Remissions both in Granulocytic Anaemias and in Agranulocytosis?—Perhaps here granulocytosis and agranulocytosis are merely secondary manifestations of a response to some evocative agent whose stressor effect is mitigated by gluco-corticoids. The condition is apparently comparable with the rise in body temperature occasioned by cortisone in Addisonian hypothermia, though the same compound depresses fever caused by a variety of pathogens. The mechanism of such dual responses remains to be elucidated.

Is the Similarity in the Pharmacological Effects of Adrenergic and Corticoid Compounds merely Coincidental?—Adrenergic compounds and corticoids share a number of actions, such as the ability to produce hyperglycaemia and hypertension, to increase muscular efficiency, and to antagonize certain types of allergic reactions. It may be significant that such varied effects are shared by hormones of the adrenal cortex and medulla, but the cause and purpose of these similarities—as those of the morphological proximity between adrenal cortex and medulla—remain obscure.

Other Miscellaneous Problems

The inhibition of wound healing and regeneration by gluco-corticoids raises the possibility that mineralo-corticoids may act inversely, but this remains to be shown.

The frequent occurrence of purulent infections (e.g., pulmonary, renal, or hepatic abscesses) in animals and the occasional development of peritonitis in man treated with

large doses of gluco-corticoids suggest that these hormones may be useful tools in the analysis of inflammations in general.

The role of the corticoids in the pathogenesis and treatment of hypertension, eclampsia, peptic ulcer, psychosomatic derangements, various types of tumours, etc., has merely been suggested by the experiments completed up to date. Further work along these lines would be highly desirable.

A.C.T.H. and cortisone substitutes are urgently needed for therapeutic purposes. The possibility of synthesizing A.C.T.H. from its constituent amino-acids is now under investigation, and it is quite possible that certain steroids of cortisone-like structure may help to decrease the high cost and increase the availability of these useful compounds.

It will also be necessary to explore systematically those drugs which could act as gluco-corticoid synergists in certain specific instances. Some such problems have already been discussed under the heading of "conditioning," but many cognate applications come to mind. For instance, it might be useful to depress granuloma formation in tuberculosis and other infectious diseases in order to expose micro-organisms to the destructive effect of antibiotics. It should be explored whether, in the absence of encapsulation and granuloma formation, micro-organisms would be more readily attacked by antimicrobial agents.

The Necessity for Specialists in Adaptation and Problems of Stress.—Finally we should like to emphasize that the science of adaptation is beginning to develop into a separate branch of medicine. Apart from specialists in certain techniques (surgery, *x*-ray, laboratory diagnosis) and target organs (heart, gastro-intestinal tract, skin, eye), we will need the specialist in stress and adaptation.

Just like his colleagues in other disciplines, he will have to borrow from cognate fields. The ophthalmologist has to acquaint himself with certain aspects of surgery, internal medicine, allergy, etc.; the cardiologist must know a good deal about *x*-ray findings, the physics involved in electrocardiography, etc. Similarly the stress specialist will have to devote a good deal of his time to the study of internal medicine, experimental physiology and pathology, allergy, neurology, endocrinology, and so forth. Nevertheless, the immensity of the subject-matter related to stress problems will undoubtedly require the training of specialists who may be consulted in connexion with diseases in which the stress factor plays a predominant part.

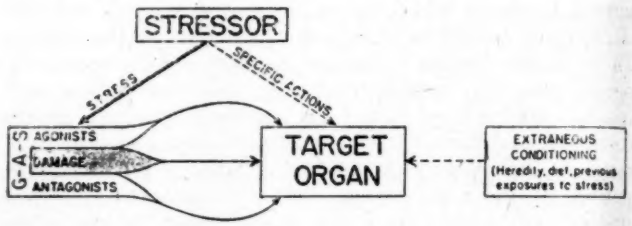
Diagrammatic Synopsis of the General Adaptation Syndrome Concept

And now in these last few paragraphs I should like to summarize concisely what appears to me the most important outcome.

All agents can act as stressors, producing both stress and specific actions. No agent can produce one without the other. The specific actions affect the target organs in a variety of ways. Stress acts only through the general adaptation syndrome. It causes defence and damage.

The defence mobilizes agonists and antagonists, which, through their interaction on the target organ, stabilize the latter and adjust its response to injury. But stress also invariably causes some degree of damage through the general adaptation syndrome. This likewise affects the target organ, though not through the humoral and nervous mediators of non-specific defence.

Factors extraneous to the general adaptation syndrome (e.g., heredity, diet, previous exposure to stress) can condition these responses. Thus in the final analysis the reaction of the target organ will depend upon the specific actions of the stressor, the effects of the resulting general adaptation syndrome (agonists, antagonists, non-specific damage), and extraneous conditioning factors. This explains how the essentially stereotypic general adaptation syndrome response can lead to a variety of polymorph syndromes and why so many apparently unrelated diseases are amenable to therapy by "stress hormones."



Disease consists of two components—damage and defence. Up to now medicine attempted to attack almost only the damaging pathogen (to kill the germs, to excise tumours, to neutralize poisons).

As regards defence, hitherto medicine limited itself to such vague advice as the usefulness of rest, wholesome food, etc. A study of the general adaptation syndrome suggests that henceforth we will be able to rely upon much more effective means of aiding adaptation to non-specific local or systemic injury by supplementing the natural defensive measures of the general adaptation syndrome whenever these are suboptimal.

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The annual "Heberden Round" was conducted by Professor F. Coste, professor of rheumatology in the University of Paris, at the Hôpital Cochin on May 20. Members of Professor Coste's unit and his associates presented cases and short papers. The president and many members of the French branch of the Ligue International contre le Rhumatisme attended, and members of the British branch were also invited. Professor Coste gave a review of his attempts to stimulate the pituitary and the adrenal glands or to produce cortisone-like effects; epinephrine, general anaesthesia, carotid sinus stimulation or infiltration with procaine, *x* rays, and short-wave diathermy directed to the glands had all been tried. He had also used androgens, oestrogens, desoxycorticosterone acetate in large doses, alone and in conjunction with ascorbic acid, and, also without effect, △-4-pregnenolone. Dr. Delbarre then showed a film illustrating the effects of A.C.T.H. in rheumatoid arthritis, and read a paper, in which he reviewed 40 cases of myelomatosis seen during the past three years. Other papers were by Dr. J. P. Amoudruz on the use of tomography of the sacro-iliac joints in early ankylosing spondylitis; Professor Merle D'Aubigne on the treatment of spondylolisthesis; Dr. J. Forestier on a type of ankylosing vertebral hyperostosis; and Dr. Mathieu Pierre-Weil on angina in rheumatoid arthritis. Dr. G. D. Kersley gave an account of an unusual case of gout and Dr. E. G. L. Bywaters described cases of the post-rheumatic arthrosis of Jaccoud. The Society was entertained to lunch by Professor Coste, and paid a visit to Enghien, where they were again entertained. A reception was also given by the British Council.

THE SO-CALLED STEVENS-JOHNSON SYNDROME

BY

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The syndrome described by A. M. Stevens and F. C. Johnson (1922) consisted of a generalized eruption, continued fever, inflamed buccal mucosa, and severe purulent conjunctivitis. It remains a rarity.

Controversy still exists about whether it is identical with the condition formerly referred to as erythema exudativum multiforme (Hebra). It has been claimed that cases of this nature were described in France as early as 1822 by Alibert and Bazin (Rosenberg and Rosenberg, 1940), but it was left to Hebra (1866) to attach a name to this group of polymorphous erythemas, which he considered due to a systemic invasion by some unknown factor. He stated that the mucous membranes may be involved, but did not stress the occurrence of conjunctivitis of a serious type.

This form was noted by Mracek (1902) and Crocker (1903), the latter mentioning that the conjunctiva may be the first membrane involved. Dühring (1896), describing over a hundred cases of erythema exudativum multiforme (Hebra), mentioned only mild conjunctivitis. J. H. Bailey (1931), in dealing with his three cases from the ophthalmological standpoint, recognized their similarity to those described by Stevens and Johnson, but also found that they resembled the much earlier cases of Fuchs, 1876; Molenes-Mahon, 1884; Gerk and Kain, 1892; Stark, 1918; Barkan, 1918; Hartler, 1921; and Raffin, 1922. The Commission on Acute Respiratory Diseases (1946) considered that the use of the eponym "Stevens–Johnson" was without historical justification.

The work of Rendu (1916) should be referred to. Under the title "Ectodermose érosive superficielle," he gave an early account of a condition differing little from that described by Stevens and Johnson.

Ginandes (1935) preferred to regard the Stevens–Johnson type cases as conforming to the atypical cases of erythema exudativum multiforme (Hebra), and concluded that a satisfactory designation of these cases would be erythema exudativum multiforme (Stevens–Johnson). He considered that this term would call attention to the unusual features of the condition emphasized by the authors. Among others who contend that the Hebra and Stevens–Johnson types of erythema exudativum multiforme are essentially the same disease are Keil (1940) and Smith (1929).

Modern Cases

The cases of Stevens and Johnson occurred in children aged 7 and 8. Ginandes (1935) described a case and reviewed the nine others that had been reported up to that time. He brought out the startling fact that total blindness had occurred in seven. The other cases had been contributed by C. A. Bailey (1929), Rutherford (1929), and Wheeler (1930). Givner and Ageloff (1941) published their cases as being exceptional in that vision had been retained.

Murphy (1944) described a case in a man aged 22, the second to be reported with penile lesions. In the ensuing cases of Erger (1944), who had reverted to an older name "erythema multiforme pluriorificialis," Kove (1945), and Hoffman and Stone (1948) genital lesions were described on each occasion, and these have come to be recognized as an almost constant feature of the severer case.

The Commission on Acute Respiratory Diseases (1946) published six cases of severe erythema multiforme with evidence of a pulmonary involvement in three, and recognized as a non-bacterial pneumonia. The chief purpose of the report was to emphasize the relationship of pneumonia to erythema exudativum multiforme, since lung involvement was a feature not stressed enough in previous descriptions. The ages of their six cases ranged beween 18 and 36 years.

Stanyon and Warner (1945) reported 17 cases of the major form of erythema exudativum multiforme, with non-bacterial pneumonia in 14, including two fatalities. Patz (1947) made a study of six cases, endeavouring to discover a virus. In his cases complement-fixation tests with psittacosis antigen were negative, as also were the findings following intracerebral and intraperitoneal injection of vesicular fluid into rabbits, guinea-pigs, and mice.

Dealing with the relationship between pneumonia and erythema multiforme exudativum, Finland, Joliffe, and Parker (1948) reported four cases and three necropsies. They investigated the cases with a view to discovering any association with psittacosis. In their first case serological examination revealed a positive complement fixation in a dilution eventually reaching 1 in 1,024. A significant rise in psittacosis antibodies was shown in Case 2, and in this and also in the third case there were histories of contact with a sick or dead bird. No inclusion bodies were seen in any of the cases, and virus studies were negative.

Anderson *et al.* (1949), dealing with a solitary case, claim to have found a virus and cytoplasmic inclusion bodies after rabbit cornea inoculation. A recent Continental report of a case was contributed by Scarzella (1949).

In Great Britain cases of erythema multiforme accompanied by severe systemic manifestations have been few and far between. A brief communication by Dowling (1940) drew attention to a group of six cases manifesting erythema multiforme with conjunctivitis, stomatitis, and genital lesions.

Nellen (1947) and Murray (1947) published full reports of cases of erythema exudativum multiforme occurring in this country. Murray's cases occurred in youths of 15 and 16 years.

Other recent English cases have been noted by Sneddon (1947), Johnstone (1947), Neale (1948), and Dresner (1949).

Present Series

In recent years I have encountered several cases of erythema exudativum multiforme. Three of them come into the same category as the Stevens–Johnson type, the others, being much more benign, conform to Hebra's type. The sixth case showed only bullous erythema multiforme, stomatitis, and mild pyrexia. There was no conjunctivitis, but the similarity otherwise to the two lesser cases has induced me to include it as a mild case of erythema exudativum multiforme (Hebra).

It has been customary in the various case reports published on the Stevens–Johnson syndrome to elaborate the negative pathological findings. In the cases here described the Wassermann reactions were negative and urinalysis and blood counts, if within normal limits, have not been dealt with *in extenso*.

Case 1

A policeman aged 27 was admitted to the Royal Gwent Hospital on February 8, 1946, complaining of sore mouth and throat, swollen neck glands, and conjunctivitis. He was a married man with no children.

His condition began with a sore throat three days previously. His voice was hoarse and there was occasional vomiting. Severe ulceration of the mouth developed, his tongue, the inner sides of his cheeks, his gums, and his lips being involved. At the same time the glands in his neck started to enlarge and severe conjunctivitis was present. There was a superficial ulcer on the glans penis and a rash on the back of his wrists and on the front of his knees.

In 1938, while working in a tinplate factory, he first developed sore mouth. Only his mouth was affected, there being no accompanying rash. This cleared up rapidly with simple treatment. He had repeated attacks of sore throat in 1939, 1940, 1941, and 1942. The diagnosis made was Vincent's angina (these may or may not have represented the earliest attacks of erythema exudativum multiforme). In 1943 the mouth ulceration was associated with a rash on his limbs, legs, lower abdomen, and penis. A diagnosis of erythema multiforme was made. He stated that he also had a conjunctivitis. The rash did not extend above the elbows and mainly covered the surface of the arms and hands; it also affected the legs below the knees. The lesions were papular and bullous, and healed in a week, intense irritation being produced initially. Similar attacks were experienced in 1944 and 1945, conjunctivitis being present each time.

On examination his temperature was 102° F. (38.9° C.) and his pulse 128. He showed a dark crusting of his eyelids and also of his mouth. His right eye was inflamed and there was a purulent discharge. The buccal mucous membrane was profusely ulcerated. As regards his skin, a few discrete erythematous nodules were present on the dorsum of the wrists and the fronts of the knees, and there was a superficial irregular ulceration of the glans penis. Swabs taken from the mouth and throat revealed Vincent's angina, and a culture of the pus from the eye grew *Staphylococcus aureus*. The red blood count was normal and the leucocytes numbered 13,900 per c.mm. A slight albuminuria was found. Penicillin therapy was started at once and in seven days his temperature fell uniformly to normal and remained normal. He was discharged on February 26 without further complication.

Case 2

A single agricultural labourer aged 26 was admitted to hospital on February 8, 1949, on account of malaise, cough, and severe skin eruption. There was no history of V.D., and his past and family histories were non-contributory. He said that on January 23 he began to feel hot and out of sorts while at work. On the 27th he returned home and took to his bed on account of what he thought was "flu." Three days later he observed the appearance of red patches on the back of both thumbs and his mouth became sore. Following this his eyes started to lacrimate and to feel irritable, and the genital eruption was first discerned.

After two days on sulphathiazole tablets he was transferred to an isolation hospital. His eruption was spreading, and by February 4 he was found to have an extensive erythema multiforme eruption chiefly of the iris type but with some commencing bullae. By this time he was seriously ill and was transferred to the Royal Gwent Hospital.

On examination he was obviously ill and had a temperature of 102° F. (38.9° C.) and a pulse rate of 104. The skin of the trunk and limbs showed dark-red discrete and confluent lesions of erythema multiforme of both the bullous and the iris forms (Fig. 1). Some of the bullae had ruptured on the back, leaving raw surfaces (Fig. 2). Both eyes showed black, haemorrhagic crusting (Fig. 3). There was a prominent bilateral mucopurulent conjunctivitis. Both corneae were clear. The pupil reactions, fundi, eye movements, etc., were all normal. A similar haemorrhagic crusting existed on both lips, and there was an extensive membranous desquamation of the lining of the mouth, producing much discomfort.

Abnormal physical signs in the chest were not pronounced at this stage, but on auscultation low and medium-pitched rhonchi could be heard. There was inspiratory crepitus at both bases. The genital lesions consisted of a superficial excoriation extending from the scrotum to the under surface of the penis. There was a purulent balanitis but no urethritis.

Progress

During the four days after admission his condition deteriorated and he became very drowsy. The skin lesions were pemphigoid and raw. Penicillin, 1,500,000 units daily in aqueous solution, was then started, and after two days he seemed

FIG. 1.—Case 2. Distribution of skin lesions.

improved. The eyelid plaques were becoming detached and the bullae over his trunk were collapsed and dry. His temperature was down and he coughed less.

FIG. 2.—Case 2. Appearance of ruptured bullae on back.

On February 17, however, the twenty-first day of his illness, his chest symptoms worsened and his temperature was swinging between normal and 102° F. (38.9° C.). Next day a patch of pulmonary consolidation was clinically discernible in the left lower zone. An *x*-ray photograph of the chest showed a diffuse opacity in the left lower lobe due to consolidation. Another opacity was present in the right cardiophrenic angle, due to consolidation of one of the segments of the right lower lobe.

FIG. 3.—Case 2. Facial appearance.

Penicillin was discontinued after 10 days' treatment, sulphathiazole being substituted. Some improvement in the chest signs took place during the next few days, and on February 22 a further *x*-ray film revealed a small quantity of fluid at the right base. There had been some clearing of the opacity at the right base, and now this area showed a honeycombed appearance. The left base also showed slight clearing. The pain in the chest had almost gone, but considerable languor and some dyspnoea remained.

From the time penicillin had been started systemically and locally the skin lesions had improved steadily, and there had been no tendency for fresh bullae to appear. The most stubborn areas were on the genitals, and these persisted for two weeks after other areas had cleared. Continued rest in bed was advocated until all lung signs had cleared, but, even after a further three weeks, clinical and radiological signs remained

and the patient then insisted on leaving hospital after 53 days because he felt so well.

At a later date he was seen in his own home and recovery was apparently complete, but even as late as May 19 examination of the chest revealed some impairment of percussion note and some residual crepitation at the left base. An *x*-ray photograph showed that there still remained obliteration of the left costophrenic angle, considered to be due either to a very small quantity of fluid or to pleural thickening. A final radiograph in September indicated complete resolution.

Pathological investigations revealed little. The blood count was normal on several occasions and the leucocytes remained at about 9,000 per c.mm. The erythrocyte sedimentation rate was 30 mm. a minute (Westergren). Examination of the sputum for tubercle bacilli was repeatedly negative. Sputum culture on February 8 showed a profuse growth of *Neisseria catarrhalis* and *Staphylococcus aureus*, coagulase-positive.

Case 3

A girl aged 5 was admitted to hospital on November 15, 1949, on account of a generalized skin eruption accompanied by

FIG. 4.—Case 3. Appearance of facial lesions on twelfth day of illness.

a purulent conjunctivitis and a severe stomatitis. Her temperature was 100° F. (37.8° C.) and her pulse 110 a minute. There was considerable prostration.

Ten days previously her doctor had been called in and found a scarlatiniform eruption and a troublesome cough. The temperature was then 102° F. (38.9° C.) and the pulse rate 100. No abnormal physical signs were detected in the chest, and sulphadiazine therapy was instituted. On the following day the rash had almost faded, but diarrhoea had begun. The cough persisted, and three days later some crepitations were discernible in the chest. The temperature was raised a little and the child appeared better. On November 13 there began swelling of the eyelids and injection of the conjunctivae and also soreness of the vulva. Next day she was considerably worse and the skin eruption was observed. The temperature had again risen to 102° F. (38.9° C.) and she was then transferred to hospital.

Physical examination revealed a very ill child resentful of being handled and muttering incoherently. There was a generalized skin eruption. On the face it consisted of confluent erythematous areas surmounted by ruptured bullae on the cheeks (Fig. 4). Irregular erythematous macules were scattered profusely over the trunk and limbs; they were evenly distributed, some of the lesions having central vesicles (Fig. 5).

The thick purulent exudate from the eyes had matted down the lids, but after twenty-four hours it was possible to open the eyes, when photophobia was apparent. There were chemosis and injection of the conjunctivae with very thick purulent exudate. The corneae were not affected. The lids showed erythema only at this stage. The lips and adjacent skin were caked in a dry, rigid dark-red mass. It was not possible to examine inside the mouth, from the reduced orifice of which a purulent discharge was emerging. On the genitals there were a circumscribed dusky erythema of the vestibule and a thick purulent vaginal discharge.

The blood count indicated 11,200 leucocytes per c.mm. Vincent's organisms were present in a swab taken from the mouth. An *x*-ray photograph of the chest revealed no abnormality. In view of the history of diarrhoea, the stools were cultured and the presence of *Shigella sonnei* was reported.

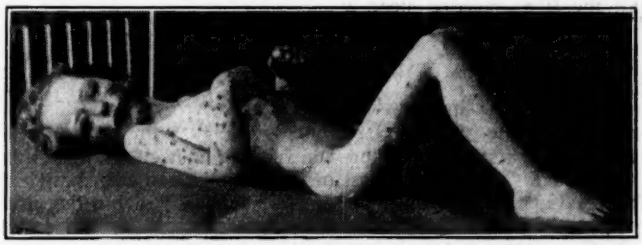

FIG. 5.—Case 3. Distribution of skin lesions.

Penicillin was given locally and systemically. Penicillin eye washes were instituted and penicillin ointment was smeared on the lids. Penicillin cream was applied to the lips and also the genitals. Sulphonamides were withheld at first, but later sulphaguanidine was given for the dysentery without untoward effects. The stomatitis proved to be the most stubborn element, and it interfered with her eating in the early stages. After being in hospital for three weeks, she would have been considered fit for discharge but for the continuing presence of dysentery bacilli in the stools.

Case 4

A girl aged 14 was seen at her home on February 2, 1949. She was complaining of soreness of the eyes and mouth, of an eruption on her hands and one foot, and of a general feeling of being out of sorts. She said that five days previously she had first noticed swelling of the upper eyelids and lacrimation. Next day her eyes had become bloodshot, and on the 4th the skin signs had started to appear on both the backs and fronts of the hands. Soreness of the mouth and lips followed and her face showed some swelling. Her temperature was slightly raised. She felt depressed and had lost her appetite. A previous attack lasted from July 10 to August 7, 1948. It was similar to the present one except that it was considerably worse.

On examination her temperature was 98.6° F. (37° C.) and pulse rate 90 a minute. Her face showed some general swelling (Fig. 6) and there was a purulent exudate from her eyes. The conjunctivae were injected and chemosed. The lips were swollen and showed a superficial ulceration, and there was a stomatitis consisting mainly of a hyperaemia of the buccal mucous membranes. The gums were swollen and brightly erythematous, chiefly anteriorly. The cervical glands were slightly enlarged, particularly on the right side. The skin

FIG. 6.—Case 4. Crusting of the lips and cervical lymphadenitis.

lesions were entirely bullous. Some had serous contents and some haemorrhagic, and a few were mixed.

Sulphathiazole was prescribed and the girl was seen again four days later. At this time she was very much improved and was up and dressed. Her face was not nearly so swollen and no conjunctivitis was evident. The bullae were subsiding, but some new erythema iris patches had appeared in the neighbourhood of the elbows and knees. During the next few days all the signs receded steadily.

Case 5

A supervisor in the Women's Land Army aged 28 was admitted to hospital on September 10, 1949, complaining of a fourth attack of a condition which showed itself as blistering of the hands and feet, redness of the genitals, and conjunctivitis. She stated that two days previously she had had burning and tingling of the lips, fingers, feet, and genitals. A rash appeared on the hands and there was vulval redness. Pain became severe in the hands and itching was unbearable.

Her first attack had come on late in June, 1949. She had taken it for mosquito bites and it subsided after only a few days. The second attack occurred two weeks later with signs on the lips, hands, and trunk, and vulval "inflammation." A further attack occurred in August, when the eyes were affected for the first time. Of significance was an attack of pain in the back and abdomen, lasting for most of January and February, 1949. There had been frequency of micturition and also haematuria. *X*-ray examination had failed to reveal any abnormality, and the condition had cleared up with the administration of sulphonamides.

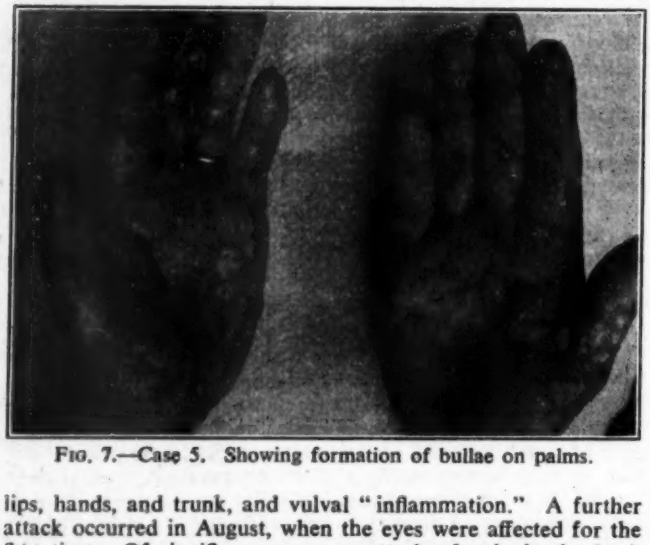

FIG. 7.—Case 5. Showing formation of bullae on palms.

There had been a chronic cervicitis since 1938 with continuing leucorrhoea. Smears were repeatedly gonococcus-negative.

On examination her temperature was 99° F. (37.2° C.) and her pulse 80. Her conjunctivae were mildly injected, but there was no indication of any purulent exudate. A few hyperaemic macules could be discerned on the lips and buccal mucosa. The whole of the palms and palmar surfaces of the fingers showed closely set erythema iris macules, confluent over the thenar eminences and some of the fingers.

Progress.—She had been taking sulphathiazole tablets for two days before admission. After having been in hospital for two days the macules on the hands developed into bullae (Fig. 7), and at the same time three blisters appeared on the lips. The manual and vulval irritation subsided and she felt more comfortable. The conjunctivitis, stomatitis, and vulvitis subsided rapidly during the next five days and she left hospital at her own request. The bullae on the hands were still prominent. The blood count and *x*-ray photograph of her chest showed no abnormal findings.

Ten days after her discharge from hospital she was seen again and was in excellent general health and spirits. Whereas desquamation was taking place at the site of the original bullae, further crops of small painless blisters were appearing on the palms of the hands.

Comment.—It was not until one further attack had occurred that light was shed on the causation of this particular case. It appeared that, for her backache, she had retained some sulphonamide tablets from the first time they had been prescribed for her, and had developed the practice of taking them during an attack. On this final occasion she had taken only one 0.5-g. tablet of sulphathiazole, when she began to experience the burning of the eyes, lips, and genitals, and to have red patches on the palms of her hands. She reported at hospital almost immediately, and the relationship between the tablets and the attacks was realized, particularly when she described how, before each earlier attack, she had taken some tablets. On this occasion the erythematous macules did not progress to bullae, and the condition subsided. No further complaint of a similar nature has been reported from this patient.

Case 6

A fitter aged 21 was admitted to hospital on June 22, 1949, complaining of an eruption on his hands and forearms and a soreness and crusting of the lips. His condition had started on June 11 with pale nodules on the skin of the hands. They were particularly sore at first until they formed blisters, which spread as high as the elbows. On June 14 his mouth was first affected.

On examination large bullae were seen on the hypothenar eminences together with dusky erythematous macules over the remainder of the palms. Purplish crusted papules, many of which were septic, were scattered on the forearms. Abundant superficial ulcers were seen on the buccal mucous membrane, and they extended on to the lips. There was a solitary crust on the right lower eyelid. The genitals were clear. At this time his temperature was 99° F. (37.2° C.) and his pulse 76.

He was given sulphathiazole, and after four days his temperature came down to normal and remained so. His blood count was normal and there were no abnormal chest signs clinically or on *x*-ray examination. He left hospital on July 2.

When seen as an out-patient on July 19 new palmar lesions were present. There were eight small pustules on the palm of the left hand. These also had completely dried in a further seven days.

Discussion

Three of the six cases described (Cases 1, 2, and 3) far exceeded the others in severity. Pyrexia was higher and more sustained, the period of illness was longer, and the clinical manifestations were more pronounced.

Careful study of recorded cases indicates that a division into mild and severe attacks is fairly constant. Reference has already been made to the suggestion by Ginandes of labelling the severe cases as "erythema exudativum multiforme (Stevens-Johnson)" and the milder ones as "erythema exudativum multiforme (Hebra)." The former have also been referred to as atypical cases of the latter. It occurs to me that simpler appellations would be "erythema multiforme exudativum major" and "erythema multiforme exudativum minor." The minor form, as originally described by Hebra, is mainly afebrile, and it involved the skin primarily. The inclusion of "continued fever" as part of their syndrome was stipulated by Stevens and Johnson, and this, together with severe conjunctivitis, provides the main points of distinction between the major and minor types of case.

A recognized feature of erythema exudativum multiforme is its tendency to be recurrent. A consideration of Cases 1 and 4 brings to light the fact that different degrees of severity may be met in different attacks in the same patient.

Before drawing conclusions from these facts, it must be emphasized that neither patient was examined clinically

at the time of the earlier attack. Accepting their histories, however, it then appears that a patient may be prone to major or minor attacks of erythema exudativum multiforme at different periods. Clearly the complaint should bear the same label on each occasion.

The sex incidence is of interest. An analysis in the major cases reveals that it is exceptional for females to be affected, and one of the few reported cases occurring in a female was described by Givner and Ageloff (1941). Patz (1947) states that one patient in five is a female. Case 3 is therefore unusual, particularly in Great Britain. The commonest age is in the early twenties. Pulmonary complications are the most threatening aspect of the condition.

As regards mortality, Lever (1944) was able to collect only four fatal cases before 1944, but many more have occurred since. Finland *et al.* (1948) mention ten deaths in addition to their own three fatalities.

The constant feature is the erythema multiforme, and the lesions are of two types—erythemato-papular and vesiculo-bullous. Attempts have been made to generalize on the distribution of these lesions. The alleged predilection for the dorsa of the hands has not been borne out by the present series—the palms have been mostly involved. Both types of lesion may be present together and the buccal mucosa is invariably affected. The size of the lesions varies within wide limits.

The failure to discover any constant abnormality is now becoming accepted. Blood counts show no marked deviation from the normal, and the examination of the urine reveals nothing further than an occasional febrile albuminuria. Animal inoculations were carried out as part of the Fort Bragg investigations, but no infective agent could be transmitted. Reference has already been made to the researches of Patz (1947) and of Anderson *et al.* (1949). *Staph. aureus* is occasionally recovered from a culture of the sputum. The organisms of Vincent's angina were found in swabs taken from the throats of Cases 1 and 3, and similar results have occasionally been noted in other cases (Chick and Witzberger, 1938). Biopsy has shown only a non-specific inflammation.

The genital lesions do not seem to form part of the general erythema multiforme eruption, but in the male cases they occur as a superficial excoriation on the glans penis and adjacent area of the sulcus and shaft.

Without being in any way specific, penicillin and the sulphonamides have been used in treatment, and quite often the beginning of the fall in temperature coincides with the administration of one or other of these agents. No dogmatic assertions can be made regarding their efficacy.

The fact that the minor attacks in Case 4 proved to be a toxic response to sulphathiazole is revealing. Case 3 had also received sulphadiazine for her initial scarlatiniform eruption. The occurrence of erythema multiforme exudativum following the administration of sulphonamides has been reported by Greenberg and Messer (1943) and Dardinski (1945), who described fatal cases of the syndrome resulting from sulphadiazine therapy. Straus (1948) also observed repeated attacks of erythema multiforme exudativum following the sulphonamide treatment of chancroid. It would thus seem to be proved that the syndrome can be a toxic drug reaction, and it is unlikely that the sulphonamides alone should be incriminated. It also seems likely that erythema multiforme exudativum can be a concomitant of virus and even bacterial infections. The association with herpes simplex (Forman and Whitwell, 1934), mumps (Kove, 1945), and primary atypical pneumonia (Stanyon and Warner, 1945) has already been noted. It may be that Vincent's angina or dysentery was the primary factor in three of the cases here described.

Summary

A historical account of erythema exudativum multiforme is given.

Published cases in U.S.A. and in this country are briefly surveyed.

Six cases of erythema exudativum multiforme are described, three being of the major (Stevens–Johnson) type and three of the minor (Hebra) type. Two of the cases were associated with Vincent's angina, one with Sonne dysentery, and a fourth was the result of sulphonamide intolerance.

The opinion is expressed that Stevens–Johnson syndrome represents only a severe form of Hebra's erythema multiforme exudativum.

Points of aetiology are discussed and the paucity of constant pathological findings is stressed.

Emphasis is laid on the possibility of non-bacterial pneumonia arising as a complication.

My thanks are due to my colleague, Dr. E. Grahame Jones, for affording me the opportunity of observing and reporting on Case 1 and for much helpful advice. For the photographs of Case 2 and for other related kindnesses I am indebted to my house-physician, Dr. Oleiwicz. The *x*-ray reports were made by Dr. T. J. Thomas, whom I also thank.

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Discussing premature babies recently, a W.H.O. committee recommended that a premature baby should be defined as one born alive with a birth weight of 5½ lb. or less. Special units for these babies should be set up where possible. W.H.O. is also sponsoring a statistically controlled demonstration in Iran on the treatment of rabies in human beings bitten by wolves.

AUREOMYCIN TREATMENT OF INFANTILE DIARRHOEA AND VOMITING

BY

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In a number of epidemics of infantile diarrhoea and vomiting that have been recorded great importance was attached to the bacteriological and virological investigations. During recent years particular interest has been aroused by a *Bacterium coli* strain, *Bact. coli* neapolitanum (B.C.N.).* Its presence was demonstrated by Bray (1945), Bray and Beavan (1948), Giles and Sangster (1948), Giles, Sangster, and Smith (1949), and by Taylor, Powell, and Wright (1949) in a number of such epidemics. Its aetiological significance has not yet been elucidated. Streptomycin treatment was given in such cases by Holzel, Martyn, and Apter (1949), but they considered that it did not exert any specific therapeutic effect. Chloramphenicol treatment was tried out by Rogers, Koegler, and Gerrard (1949) in a small number of cases, and they found the results to be encouraging. The present preliminary report covers two epidemics in which the presence of B.C.N. could be demonstrated. Eight of the patients in the second epidemic were treated with aureomycin.

Present Series

The series consists of infants treated in the Sachs Hospital for Children between July and November, 1949. On two occasions an epidemic of dyspepsia broke out among them. The first was during July–September. Altogether 20 infants were examined with respect to the presence of B.C.N. in the stools and the respiratory tract. The second epidemic started at the end of September and continued during October and November. Fourteen infants were affected. On both occasions the control material consisted of children in hospital during the same time but with no dyspeptic symptoms.

The presence of B.C.N. was demonstrated in 19 cases in the first epidemic and in all in the second. In the control series, consisting of altogether 40 children, B.C.N. bacteria were found in the stools of one child only. In the first epidemic all the children became affected during their stay in hospital, and in the second epidemic 10 became affected during that time. Of the three infants admitted to hospital for diarrhoea, one had been treated at another children's hospital two weeks earlier and two had been at a home for post-natal care.

It is of considerable interest that in our series the strain was also found in the respiratory tract (see Table I). Special note should be made of the fact that it was relatively often found in the nose. This is in view of the recent investigations of so-called dangerous carriers, in which it could be shown by Laurell (1950) that those with coliform bacteria in the nose most easily spread the infection to their surroundings.

*The strain has also been described under the name of *Bact. coli* D 433 and B.G.T. (Bray, Giles, Taylor). Kaufmann classified the strain as O 110, B 4 in Kaufmann-Vahlne's coli antigen list.

TABLE I

	Coliform Bacteria in Throat Only	B.C.N. in Throat Only	Coliform Bacteria in Throat and Nose	B.C.N. in Throat and Nose
Infants with dyspepsia:				
Epidemic I	7	3	7	5
Epidemic II	3	—	7	7
Infants without dyspepsia:				
Epidemic I	3	—	2	—
Epidemic II	11	—	2	—

The incubation time could be determined approximately in the case of 17 infants. In no case did it exceed 17 days, nor was it less than 4 days. In the majority of instances it varied between 8 and 12 days.

The clinical picture was the same in both epidemics, the main symptom being more or less severe gastro-enteritis usually accompanied by vomiting. In the first epidemic, with 5 deaths, 12 cases were regarded as severe or moderately severe and 8 as mild. In the second epidemic, in which no deaths occurred, 11 infants were seriously ill and only 2 had mild symptoms. All the infants were less than 1 year of age and 22 less than 1 month. It is of interest to note that 12 of the children affected (5 in the second epidemic) were admitted to hospital for prematurity. In conformity with the findings of Taylor, Roberts, and others, the youngest infants were commonly those most severely affected. In order to illustrate the clinical picture in more detail, accounts of two typical cases are given.

Typical Cases

Case A.—A newborn girl was admitted on the grounds of prematurity; weight at birth, 1,550 g. Nothing of note occurred during the first week in hospital. On the 11th day after admission there was slight diarrhoea, with a failure to gain in weight. Penicillin and "elkosin" therapy was started and aminosol glucose and Darrow's solution given subcutaneously. During the subsequent days there was a temporary improvement with a gain in weight. On the 23rd day there was a sudden exacerbation with increasing diarrhoea. Streptomycin therapy was started and fluids given intravenously. The condition nevertheless continued to deteriorate, the diarrhoea became watery and extremely severe, and death ensued on the 40th day. Pure cultures of B.C.N. were found in the stools seven days before death. Necropsy revealed no pathological condition in the intestines, but there was bilateral bronchopneumonia as well as bilateral purulent mastoiditis; clinically, the infant died from an acute intestinal infection.

Case B.—A newborn boy was also admitted on the grounds of prematurity; weight at birth 2,370 g. Initially there was nothing of note, but on the seventh day in hospital frequent defaecations and a loss in weight began. Sulphonamide was given by mouth, penicillin intravenously, plentiful fluids (Darrow's solution and aminosol glucose) subcutaneously, and breast milk, arobon, and glucose solution by mouth. There was no improvement; on the contrary a marked exacerbation occurred on the 13th day after admission, with pronounced symptoms of shock, bad colour, depression of the fontanelle, appreciable loss of weight, and 10 to 13 watery, violent, and mucous defaecations a day as well as frequent vomiting. He was put in an oxygen tent, streptomycin being administered by mouth and serum intratibially. During the following week his general condition varied, but there was no marked improvement. The administration of sulphonamide and antibiotics was therefore stopped. B.C.N. was found in the stools on the 17th day of illness and in the nose and stools on the 28th day. An intravenous cannula had been inserted earlier (on the 20th day of illness), and during the next six days he was mainly nourished in this way. There was then a rapid progress with a considerable

gain in weight and an improvement in the stools. The improvement continued and the patient was discharged from hospital with a weight of 2,560 g.

Treatment

During the first few days after the development of gastro-enteritis fluids were given liberally in the form of plasma, aminosol glucose, and Darrow's solution subcutaneously or intravenously and arobon and carrot soup by mouth. The basic food was breast milk.

Penicillin and sulphonamide compounds were tried in the majority of cases in both epidemics, but they had no effect on the gastro-intestinal symptoms. We noted, as did Rogers *et al.* (1949), that in several cases the gastro-enteritis had its onset in the course of penicillin and sulphonamide therapy. Streptomycin was given as well in 17 cases, but no specific therapeutic effect was seen. In this respect our results were in agreement with those reported by Holzel *et al.* (1949) and by Rogers *et al.*

"Aureomycin" Therapy

As mentioned earlier, eight patients in the second epidemic were treated with aureomycin after it had been found that the bacteria were sensitive to this antibiotic. The resistance varied inappreciably, and lay between 0.16 and 0.6 μg./ml. (resistance tests made in thioglycollate broth). The aureomycin was given by mouth in doses of 25 mg. six times a day. The results of the bacteriological investigations to determine the presence of B.C.N. after the inception of aureomycin therapy are given in Table II.

During the first few days after the institution of treatment coliform bacteria were found that were not identical with B.C.N. These also disappeared later and *Monilia albicans* was then the micro-organism most often encountered both in the stools and in the respiratory tract. *Pseudomonas pyocyanea* was found in three of the infants. These bacteria gave rise to no pathological symptoms. The clinical improvement in connexion with aureomycin therapy was striking. In order to illustrate the effect of treatment the most important clinical data are assembled in Table III and a brief account is given of the course of the illness in the patients treated.

Case 1.—The patient, a newborn infant, was admitted to hospital on the grounds of prematurity. After 17 days, in the course of penicillin treatment, he became ill with acute gastro-enteritis, manifested in vomiting and frequent watery defaecations. The constitutional disturbances became increasingly evident, the abdomen was moderately distended, and the colour ashen-grey. Streptomycin therapy was started and fluids given subcutaneously. As there was no improvement after three days and B.C.N. had been found on culture from the faeces, aureomycin treatment was begun. After 24 hours' treatment the stools were of half-solid consistency but still frequent. From the fourth day of treatment there was a good daily increase in weight and the stools were normal.

Case 2.—The patient, a newborn infant, was admitted to hospital for debility. After 12 days, in the course of penicillin therapy, gastro-enteritis developed, with frequent watery defaecations, vomiting, and loss of weight. The colour was ashen-grey and constitutional disturbances were present. Streptomycin therapy was started and fluids were given subcutaneously. B.C.N. was then found in the stools. There was a successive marked exacerbation, and streptomycin was therefore withdrawn on the fourth day and replaced by aureomycin. During the subsequent 24 hours the condition was unchanged, but after this time the stools became considerably firmer and less frequent and vomiting ceased entirely. From the fifth day of treatment the faeces were normal and there was a satisfactory daily gain in weight.

Case 3.—A 2-day-old girl was admitted on the grounds of prematurity. After 10 days her motions were frequent and loose. Although her general condition remained good and the gain in weight was satisfactory, penicillin and streptomycin were given as well as fluids subcutaneously. Her

TABLE II.—*Presence of B.C.N.*

Case No.		No. of Positive Tests Before Treatment	Day of Treatment with Aureomycin												
			1*	2	3	4	5	6	7	8	9	10	11	12	13
1	Fauces + nose	3	+	0	0	0	0	0	0	0	0	0	0	0	0
	Stools	3	+++	+	0	0	0	0	0	0	0	0	0	0	0
2	Fauces + nose	1	+++	++	++	+	++	+	+	+	0	0	0	0	0
	Stools	1	+++	+++	0	0	0	0	0	0	0	0	0	0	0
3	Fauces + nose	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Stools	2	+++	0	0	0	0	0	0	0	0	0	0	0	0
4	Fauces + nose	2	++	0	0	0	0	0	0	0	0	0	0	0	0
	Stools	2	+++	+	+	0	0	0	0	0	0	0	0	0	0
5	Fauces + nose	4	++	++	0	0	+	+	+	0	0	0	0	0	0
	Stools	6	+++	++	0	0	0	+	0	0	0	0	0	0	0
6	Fauces + nose	1	+	0	0	0	0	0	0	0	0	0	0	0	0
	Stools	1	+++	0	0	0	+	0	0	0	0	0	0	0	0
7	Fauces + nose	6	+++	0	0	0	0	0	0	0	0	0	0	0	
	Stools	7	+++	+++	0	+	0	0	0	0	0	0	0	0	
8	Fauces + nose	0	0	0	+	+	0	++	0	0	0	0	0		
	Stools	1	+++	+	+	0	0	0	0	0	0	0	0		

+++ = Plentiful. ++ = Moderate. + = Sparse (enrichment performed). 0 = B.C.N. not demonstrable (enrichment performed). * The first day of treatment denotes the day on which aureomycin therapy was started.

TABLE III.—*Clinical Data*

Case No.	Sex	Age in Days	Weight	Reason for Admission	Severity	Days after Admission before Onset of Gastro-enteritis	Complications	Intravenous Alimentation	Results
1*	M	1	1,480 g.	Prematurity	Severe	17	Sore buttocks	No	Recovered
2*	F	1	2,010 g.	"	"	12	" "	"	"
3*	F	2	1,980 g.	"	"	10	" "	"	"
4*	F	2	1,990 g.	"	"	15	" "	"	"
5	F	18	2,620 g.	Gastro-enteritis	"	On admission	" "	Yes	"
6*	M	2	2,550 g.	Delayed emptying of stomach	"	14	None	"	"
7	M	22	2,790 g.	Gastro-enteritis	"	On admission	Sore buttocks	No	"
8	M	1	1,480 g.	Prematurity	"	8	" "		"

* In none of these cases could B.C.N. be demonstrated before the onset of gastro-enteritis.

general condition gradually deteriorated and the stools became still looser and more frequent. As B.C.N. was found to be present in them, aureomycin was given. During the first four days there was still some loss of weight, but thereafter rapid improvement ensued with a satisfactory daily gain in weight.

Case 4.—This patient, a twin sister of Case 3, was also admitted for debility. Her development was at first normal, but after two weeks there was a sudden acute onset of gastro-enteritis with frequent watery motions, vomiting, and a loss of weight. B.C.N. was isolated on culture and aureomycin therapy was started on the second day. After 24 hours the stools were of half-firm consistency and the loss of weight ceased. From the fourth day of treatment there was a satisfactory daily gain in weight and the stools were firm in consistency.

Case 5.—An 18-day-old baby girl had suffered from vomiting and frequent mucous or watery motions for a week before admission to hospital. At the onset of the illness she was in a home for post-natal care. B.C.N. was found in the faeces on the day of admission. At first streptomycin and penicillin were given as well as fluids by the intravenous route. There was an initial improvement for a few days, but thereafter a marked exacerbation with vomiting and increasingly abnormal motions. Aureomycin therapy was started, and as soon as 48 hours later the stools were half-firm and a satisfactory gain in weight was noted. Improvement continued and the faeces rapidly became normal.

Case 6.—A 2-day-old boy was admitted to hospital for dyspepsia and mucous defaecations. Examination revealed delayed emptying of the stomach, but repeated cultures failed to demonstrate the presence of B.C.N. in the faeces. Penicillin was administered as well as fluids subcutaneously. There was gradual improvement, but after 14 days an acute exacerbation occurred with vomiting and loose stools. Culture then revealed B.C.N. in the faeces, and aureomycin therapy was therefore started. The stools rapidly became normal, but frequent vomiting still occurred and the loss of weight continued. Only after persistent plentiful administration of fluids intravenously did the general condition improve and an increase in weight take place. The protracted course of the illness is presumably to be ascribed to the basic disorder.

Case 7.—A 22-day-old boy had suffered from vomiting and mucous defaecations for one week before admission with an appreciable loss of weight from 3,430 g. to 2,790 g. During the first week of life he was at another hospital for children. On admission he was pale and dehydrated, and there was slight peripheral cyanosis. Oidium was present in the oral cavity. The abdomen was distended and blood oozed from the umbilicus. There was violent watery diarrhoea and vomiting. Fluids were administered intravenously, but he got worse and the loss of weight continued. The presence of B.C.N. was demonstrated already on the day of admission, but aureomycin was not given until the seventh day of illness. After 48 hours the stools became normal and the increase in weight satisfactory. Improvement continued.

Case 8.—A 1-day-old boy was admitted because of prematurity. Apart from the difficulty of keeping his temperature up, there was nothing of note the first week. On the eighth day he became acutely ill with vomiting and watery diarrhoea. The abdomen was distended and his colour was ashen-grey. B.C.N. was present in the stools and aureomycin therapy was started next day. After 24 hours a definite improvement could be noted, and after three days' treatment the stools were normal and the gain in weight satisfactory.

Summary

An investigation at the Sachs Hospital for Children in Stockholm revealed the presence of a special strain of *Bact. coli*—that is, *Bact. coli neapolitanum* (B.C.N.)—in the stools and at times in the respiratory tract of babies suffering from infantile diarrhoea and vomiting. This agrees with the findings of other authors. Eight of the patients were treated with aureomycin. Its effect was marked. Even after a few doses the B.C.N. present in the stools before the inception of treatment could no longer be found. Only in a few cases did it persist somewhat longer in the respiratory tract. Parallel with this bacteriological effect there was an improvement in the clinical condition.

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NITROUS OXIDE ANAESTHESIA WITHOUT HYPOXIA

BY

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Nitrous oxide possesses many qualities which meet both the clinical and the physical demands for a safe anaesthetic. The ever-present explosion hazard with the inflammable anaesthetics has been increased by the surgical trend towards greater use of the high-frequency electro-surgical unit and has challenged the anaesthesiologist to provide general anaesthesia with non-inflammable and non-explosive agents of low toxicity.

Neff, Mayer, and Perales (1947), in a preliminary report, outlined a method of potentiating the anaesthetic action of nitrous oxide by the intravenous administration of "demerol" (pethidine hydrochloride). Thompson (1950), in an experimental and clinical investigation of two new analgesics closely related to pethidine, during nitrous oxide anaesthesia compared the effects of these drugs with morphine and pethidine. Neff and Thompson (1948) later concluded that these new analgesics were less satisfactory than pethidine for fortifying the anaesthetic action of nitrous oxide. Mushin and Rendell-Baker (1949) confirmed the efficacy of pethidine for the supplementation of nitrous oxide anaesthesia, and Brotman and Cullen (1949) emphasized its usefulness in geriatric anaesthesia.

An extensive study of the problems incident to the use of nitrous oxide and pethidine anaesthesia has been in progress for the past five years. During this period nitrous oxide anaesthesia has been employed for all kinds of intra-abdominal, intrathoracic, and other extensive operations. Experience gained through the administration of nitrous oxide on several thousand occasions since the preliminary report has provided the stimulus to attempt to review and re-evaluate the present status of this gas.

Nitrous Oxide Anaesthesia without Oxygen Restriction

Modern anaesthesia with gases or volatile liquids presupposes a combination of these agents with oxygen. One uses the terms ether anaesthesia, cyclopropane anaesthesia, and chloroform anaesthesia, but in the case of nitrous oxide the more cumbersome and very often less descriptive

expression nitrous oxide and oxygen is more common. Preference is here given to the designation nitrous oxide anaesthesia.

One of the masters, Dr. Wesley Bourne, was so convinced of the value of nitrous oxide without oxygen restriction that he actually induced anaesthesia for dental operations with a mixture containing higher than atmospheric proportions of oxygen. Clinical and laboratory evidence was offered (Raginsky and Bourne, 1934) to support his contention that nitrous oxide with 20% oxygen could produce anaesthesia for operations not requiring great muscular relaxation. The induction of anaesthesia using nitrous oxide with a high complement of oxygen has in recent years received little attention.

Paul Bert (1878) reported on the harmlessness of nitrous oxide for prolonged administration to animals when a mixture of five parts of nitrous oxide to one part of oxygen was given under one and one-fifth atmospheres of pressure. Referring to the degree of anaesthesia obtained, he stated : "In this condition the animal after a couple of minutes of agitation is completely anaesthetized. The corneal reflex disappears ; you can pinch a sensitive nerve and do an amputation without any movement of the animal ; the muscular relaxation seems extraordinary, and if the regular respiratory movements were not present you could think him dead. It can last one-half hour to one hour without any change. The blood is of normal red colour, rich in oxygen, the heart strong, and the pulsations normal. At the same time excitation of any centripetal nerve will give the same results as on a normal animal. When you take off the bag with the gas after three or four inspirations of the free air the animal gets back the sensitivity, intelligence, independence, and tries to bite rather often. As soon as the ties are off it runs away and seems gay and vivacious."

Henderson, Brown, and Lucas (1927) were unable to duplicate Paul Bert's results with nitrous oxide and oxygen under pressure, and concluded that oxygen lack was a necessary accompaniment of anaesthesia with this gas. Most pharmacologists and many anaesthetists accepted their results as conclusive evidence that, although nitrous oxide did possess some analgesic properties, it was not an anaesthetic unless its administration was accompanied by periods of oxygen restriction.

Faulconer, Pender, and Bickford (1949) demonstrated rather conclusively in man that the depth of anaesthesia produced by nitrous oxide in the presence of excess oxygen is directly proportional to the partial pressure of the anaesthetic gas. They were able to demonstrate the soundness of Paul Bert's reasoning when he projected the results of his animal experiments into clinical application as follows : "The fact that anaesthesia could be obtained only by the inhalation of pure nitrous oxide means that for a sufficient saturation of the organism it should be in a tension equal to one atmosphere. Under normal pressure it means a proportion of the gas of 100%. If we could place the patient in an apparatus where the pressure would be two atmospheres we could obtain the necessary pressure of the gas by using a mixture of 50% nitrous oxide and 50% air ; in this way it will be possible to attain sufficient anaesthesia with a normal amount of oxygen in the blood and a normal respiration."

Object of Oxygen Restriction during Nitrous Oxide Anaesthesia

Oxygen restriction during nitrous oxide anaesthesia was directed mainly towards the attainment of relaxation of the skeletal musculature. Nitrous oxide combined with oxygen in atmospheric proportions will usually result in only a very moderate degree of muscular relaxation in the adequately premedicated patient. Superimposing oxygen lack will result in additional relaxation. Severe hypoxia will cause the muscles to become rigid.

Oxygen lack is often considered to be the only important factor in the response of the patient to nitrous oxide when the oxygen concentration falls below atmospheric proportions. The fact that the replacement of oxygen with nitrous oxide produces slightly more profound anaesthesia is often overlooked. The response of the patient must be attributed to a combination of drug action plus oxygen lack. The reduction of the oxygen concentration by 1 or 2% will not adversely affect the average patient, and yet it might afford the additional depth needed to avoid the administration of other less readily eliminated drugs. In practice it appears best arbitrarily to limit this reduction in oxygen concentration to 2% below its concentration in the atmosphere. The muscles may become somewhat relaxed but never flaccid as a result of so moderate a reduction in oxygen tension. Flaccidity can be accomplished only by expanding the lungs with oxygen immediately after a period of severe hypoxia.

The introduction of curare into anaesthesiology has provided the anaesthetist with an agent by means of which muscular relaxation may be provided during light surgical anaesthesia.

Use of Oxygen in Higher than Atmospheric Proportions

There is no good reason to believe that because 20% oxygen is good for the body economy 30, 40, or 50% is better, unless there is evidence of pre-existing hypoxia. An excess of oxygen will not ensure good ventilation in the patient who is suffering from depressed respiration and a consequent accumulation of carbon dioxide. The higher the oxygen concentration the lower the nitrous oxide and the weaker the anaesthetic, and the greater will be the demand for supplementation with other agents. Oxyhaemographic studies support the clinical observation that it is more rational to increase the proportion of nitrous oxide than arbitrarily to maintain oxygen in excess and therefore be obliged to administer larger doses of hypnotics, narcotics, or muscular relaxants than would otherwise be required for light anaesthesia.

Analgesic Properties of Nitrous Oxide

The subjective nature of analgesia makes its evaluation rather difficult, and yet it is of fundamental importance in the study of an anaesthetic of relatively low potency such as nitrous oxide.

Seevers, Bennett, Pohle, and Reinardy (1937) studied the action of sub-anaesthetic concentrations of nitrous oxide in man. They found the optimum concentration of nitrous oxide for continuous inhalation which would produce a maximum degree of analgesia and yet retain the co-operation of the subject to range between 35 and 40%. Bennett and Seevers (1937) found that there was little difference in the analgesic action of nitrous oxide whether diluted with oxygen or with air. Their results indicated that if there is any difference better analgesia is obtained when oxygen is the diluent. They also showed that the greatest reduction in pain sensitivity occurs within the first five minutes, with the greatest elevation of the threshold in ten minutes.

The demonstrated analgesic property of nitrous oxide offers further proof that oxygen lack does not account for the pain-relieving qualities of the gas, and may even interfere with the production of anaesthesia.

Rapid Induction of Anaesthesia

The rapid induction of anaesthesia with nitrous oxide required oxygen exclusion for its success. This requirement was readily admitted by McKesson, a leading exponent of the method, who did not believe that short periods of even complete oxygen lack were necessarily harmful. When nitrous oxide is administered without oxygen the induction may be smooth, but with the addition of oxygen in atmospheric proportions anaesthesia lightens and the more vigorous patients will enter the stage of delirium. It would appear that oxygen lack so limits the time available that adequate tissue saturation of nitrous oxide is not accomplished by this method despite the higher partial pressure.

Compromise Induction of Anaesthesia

Some anaesthetists, not having sufficient confidence in their ability to induce anaesthesia without oxygen restriction and at the same time being fearful of the rapid induction with pure nitrous oxide, try to effect a compromise. The usual procedure is to administer first a combination of nitrous oxide with 6 or 8% oxygen. One has only to compare the loss of consciousness incident to the inhalation of 100% nitrous oxide with the unpleasant subjective sensations associated with the slow development of oxygen lack to realize why this manner of induction is usually very unsatisfactory. Sensations of shortness of breath, suffocation, or choking are not entirely compatible with mental tranquillity.

The patient struggles, whereupon the oxygen consumption of the body increases fourfold to eightfold. The anaesthetist responds to the struggling of the patient by further reducing the oxygen in the anaesthetic mixture in order to "get him deeper"; the demand for additional oxygen is met by restriction. Finally, the patient loses consciousness, but slight muscular twitchings may be observed around the face, while the larger skeletal muscles begin to stiffen. The addition of oxygen at this point renders the patient less rigid at once, although not well relaxed.

Slow Induction of Anaesthesia

The slow induction of nitrous oxide anaesthesia was advocated by Guedel in 1922. At that time he stated: "Rapid induction of nitrous oxide is a heritage of the past. Anaesthesia as a rule is smoother as induction is slower." Later in the same article, referring to difficulties encountered in the "so-called stimulated types," he went on to say: "Time and oxygen should be the rule for these cases. The time necessary in some extreme cases to consummate a nice induction may be ten or fifteen minutes. If fifteen minutes is not enough time take more. Maintain ample tissue oxygenation while allowing time for the nerve-cell absorption of the nitrous oxide, and it is probable that any patient will be quietly anaesthetized and will like the sensation."

In the presence of adequate oxygen the time of induction is not limited, and despite the lower partial pressure the maximum tissue concentration compatible with safety is ultimately achieved.

Breathing nitrous oxide with a high complement of oxygen promotes a receptive attitude on the part of the patient to the anaesthetist's reassuring remarks. It is rather difficult for the anaesthetist to gain the patient's confidence while forcing him to breath a choking gaseous mixture. The faith which the patient has in the anaesthetist as a result of the pre-anaesthetic visit may be destroyed in a few suffocating moments.

Pre-oxygenation

Pre-oxygenation with 100% oxygen for five or ten minutes before the addition of nitrous oxide facilitates the induction of anaesthesia. The optimum action of nitrous oxide seems to be more quickly effected if the patient is first permitted to breath pure oxygen. It is possible that this may be explained on the basis of an initial elimination of some of the body nitrogen, reducing the tension of this gas in the alveoli and allowing a corresponding increase in space for nitrous oxide. The concentration of nitrous oxide may be rapidly or slowly increased, and as long as the percentage of oxygen is held near atmospheric the patient will not experience the unpleasant sensations associated with hypoxia. Many patients show an initial rise in blood pressure of approximately 10 mm. of mercury as the face mask is applied, although 100% oxygen is being delivered at a brisk flow rate. The blood pressure rapidly assumes its pre-existing level as the patient becomes accustomed to the face mask. Usually no further increase occurs as nitrous oxide is introduced. It is worthy of note that when nitrous oxide is slowly added first-plane anaesthesia usually occurs within ten minutes and while the oxygen concentration is still 40 or 50%.

Elimination of carbon dioxide will prevent the occurrence of subjective disturbances incident to its accumulation in the respired atmosphere. Rebreathing without carbon dioxide elimination may cause the patient to be conscious of a feeling of impending suffocation, even though the oxygen concentration of the inspired mixture is abnormally high.

Supplementation of Anaesthesia

In view of the foregoing evidence, which strongly suggests that the depth of nitrous oxide anaesthesia is limited entirely by the oxygen requirements of the body, it is reasonable for the anaesthetist to try to gain the full benefit of the action of nitrous oxide independent of oxygen lack before considering its supplementation with drugs whose action is less readily reversed. At the present time we are not in a position to take clinical advantage of the increased depth of anaesthesia produced by administering nitrous oxide under a significant positive pressure, but we can realize the benefits of slow induction and pre-oxygenation. Supplementation will usually be required to provide adequate reflex obtundation with an 80/20% mixture of nitrous oxide and oxygen.

Since the preliminary report (Neff, Mayer, and Perales, 1947) in which pethidine ("demerol"; ethyl-1-methyl-4-phenylpiperdine-4-carboxylate) was recommended for the supplementation of nitrous oxide anaesthesia, we have experimented with and, later, clinically employed two of its analogues for this purpose. These drugs—namely, "bemidone" (ethyl-1-methyl-4 (3-hydroxyphenyl) piperdine-4-carboxylate hydrochloride) and "ketobemidone" (ethyl-1-methyl-4 (3 hydroxyphenyl) piperdine-4-ketone hydrochloride)—proved to be considerably more powerful as analgesics than pethidine. Bemidone proved to possess twice the analgesic activity, milligram for milligram, of pethidine, while ketobemidone was approximately 15 or 20 times more powerful. The respiratory depression resulting from comparable analgesic doses indicated that they possessed no significant advantages over pethidine. Dolophine was tried as a supplement to nitrous oxide anaesthesia in dogs, and the respiratory depression associated with its intravenous administration was so great that it was considered to be unworthy of clinical trial.

In reviewing the records of the supplemented nitrous oxide anaesthetics administered during the past eight

months some outstanding developments were observed. First, the dose of pethidine was approximately one-half the amount used five years ago. Secondly, in operations lasting over three hours 50% or more of the total dose of pethidine was given during the first hour. One of the reasons for the reduction in the amount of pethidine used was the substitution of ether supplementation for pethidine and curare for endotracheal intubation in extensive surgical operations. In those cases not requiring endotracheal intubation the practice of first obtaining the full effect of nitrous oxide before pethidine supplementation has been a factor in the successful employment of smaller doses of this drug. In all cases it was found that the average dose level for any particular type of operation, such as cholecystectomy, pneumonectomy, or fenestration, could be reduced by closer attention to the response of individual patients to small amounts of pethidine. In many instances where we formerly gave an initial dose of 50 mg. of pethidine we subsequently found that 20 or 30 mg. was often satisfactory. In other cases additional amounts of 10 mg. were needed to obtain the desired effect.

Maintenance of Anaesthesia

Nitrous oxide supplemented with pethidine, plus curare in cases requiring muscular relaxation, will provide satisfactory anaesthesia for most surgical operations. Where ether was used to facilitate endotracheal intubation the anaesthetic mixture was found to be sufficiently free of ether to be non-explosive within ten minutes of its discontinuance, provided the period of its administration did not exceed eight minutes. Tests for explosibility were made with the Mine Safety Appliance Company's explosimeter.

Anaesthesia was maintained with a continuous flow of an 80/20% mixture of nitrous oxide and oxygen. Carbon dioxide was eliminated with soda-lime by the to-and-fro method. The oxygen concentration was checked at frequent intervals by the Beckman gas analyser. The usual flow rates of the gases were 4 litres per minute for nitrous oxide and 1 litre per minute for oxygen. These flow rates were, as a rule, doubled before, during, and for a short time after any interruption in the anaesthesia for the insertion of an airway or the changing of a canister. It is advisable to limit so far as possible the number of interruptions in the anaesthesia during the maintenance period. A pharyngeal airway should be inserted early in all cases, whether the patient appears to require one or not. In operations such as lobectomy for bronchiectasis, where frequent interruptions in the anaesthesia are necessary for the recovery of secretions, nitrous oxide anaesthesia is probably contraindicated.

Intra-abdominal Operations

Extensive intra-abdominal operations performed under nitrous oxide anaesthesia require less pethidine supplementation for the control of traction reflexes when the patients are given the benefit of a splanchnic block with 60 ml. of 1% procaine with adrenaline in 1 in 200,000 concentration. For example, the average gastric resection lasted four hours in nine cases chosen at random. The average dose of pethidine per case was 131 mg. In one case lasting three hours in a patient who was given a splanchnic block the total dose of pethidine was 50 mg. The average dose of curare administered to these patients was 140 units or 21 mg. of *d*-tubocurarine, and the patient who received the splanchnic block required 120 units or 18 mg. of *d*-tubocurarine. As might be expected, when curare is administered only for the purpose of obtaining muscular relaxation, the required dose will vary very little in those patients who have received and those who have not received a splanchnic block. The dose of pethidine, on the other hand, is appreciably reduced by the block.

Intrathoracic Operations

Nitrous oxide was used for all kinds of intrathoracic operations, with several notable exceptions. Ether anaesthesia with the highest possible percentage of oxygen was considered more suitable for the Blalock operation for pulmonary stenosis, where a patient already suffering from oxygen lack must be subjected to additional hypoxia during the operation. Supplementation of nitrous oxide anaesthesia with non-volatile drugs in order to permit an extremely high concentration of oxygen must be of such magnitude as to render the nitrous oxide almost impotent.

The unsuitability of nitrous oxide for patients undergoing lobectomy for bronchiectasis has already been mentioned, and the advantages of the slower emergence from ether anaesthesia should be emphasized.

In 24 consecutive operations, including 5 patent ductus operations, 10 transthoracic oesophageal and gastric resections, 2 diaphragmatic herniorrhaphies, 3 pneumonectomies, 3 exploratory thoracotomies, and 1 resection of a mediastinal tumour, only 12 received any curare. The average duration of these operations was 2.7 hours and the average dose of pethidine was 79 mg., or 28 mg. an hour. In the 12 cases in which curare was administered the average dose was 100 units or 15 mg. of *d*-tubocurarine, or 5.25 mg. an hour.

Recently it has been found that nerve block of the sympathetic chain, the phrenic, and the vagus under direct vision will provide better operating conditions and ensure greater freedom from traction reflexes than can be obtained directly from profound anaesthesia or indirectly by the use of curare.

Other Operations

Of 100 consecutive extra-abdominal and extrathoracic operations 25 required more than three hours of anaesthesia. The procedures included radical mastectomies, laminectomies, radical neck dissections, and extensive orthopaedic procedures.

Nine of the 25 patients were given a thiopentone induction, while the remainder were not. It is interesting to note that, while the average dose of pethidine for all cases was 30 mg. an hour, 37 mg. an hour was the average dose for the patients who received a thiopentone induction. This might reasonably be explained on the basis of slower saturation of nitrous oxide incident to the respiratory depression of thiopentone.

Premedication.—Adult patients rarely received doses of morphine exceeding ¼ gr. (11 mg.) combined with 1/150 gr. (0.43 mg.) of scopolamine one and a half hours preoperatively. A short-acting barbiturate was administered the night before operation.

Recovery from Anaesthesia

Recovery from nitrous oxide anaesthesia is almost immediate when it has not been complicated with hypoxia. Patients who have received pethidine supplementation during nitrous oxide anaesthesia regain their mental faculties before perceiving pain. In those cases in which pethidine has not been given, post-anaesthetic analgesia is rarely a feature of nitrous oxide anaesthesia. Emergence delirium, a rather common complication of thiopentone hypnosis, cyclopropane anaesthesia, and nitrous oxide complicated with hypoxia, has not been noted in any case

The cough reflex returns quickly after the termination of the anaesthesia. The early return of this reflex is in agreement with the general observation that pethidine is rather ineffective in causing its abolishment. Control of cough with pethidine during nitrous oxide anaesthesia is probably due to the slightly greater depth of anaesthesia which it provides, and when the nitrous oxide is discontinued pethidine itself will not inhibit the cough reflex.

The pharyngeal reflex usually becomes active only after consciousness has returned. Many patients do not object to the presence of a pharyngeal airway even after they awaken. On request they will open their mouth to facilitate its removal.

Summary

A further report on nitrous oxide independent of oxygen restriction has been presented.

The factors which we consider important, based on our experience in over 2,000 administrations for all kinds of operations, including intra-abdominal and intrathoracic procedures, have been emphasized.

Pethidine and curare continue to be the preferred drugs for enhancing respectively the reflex obtunding and relaxing qualities of nitrous oxide.

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PROLONGATION OF THE INITIAL STARVATION PERIOD IN PREMATURE INFANTS

BY

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Prematurity still ranks high among the causes of neonatal death. Its prevention is a matter of obstetric concern. The successful rearing of a premature infant is one of the paediatrician's major tasks, and any method of removing one of the hazards associated with prematurity is worthy of consideration. The special hazards operate particularly in the first three days of life, during which period about 75% of the fatalities occur. Intracranial trauma, congenital malformations, and atelectasis may be beyond therapeutic care, but asphyxia following inhalation of fluid—which is a common cause of death—can be avoided if no fluid be given during these first few days.

It is the purpose of this paper to describe the rationale and the routine followed in the care of a group of premature infants weighing between 2 and 5 lb. (0.9 and 2.3 kg.) at birth.

Premature infants may suffer considerable shock at birth and their immature respiratory centres be further adversely affected by anaesthetics or analgesics administered to the mother as well as by cerebral oedema or actual intracranial haemorrhage. The sucking reflex may be absent and the swallowing and coughing reflexes inadequate. As a result a spill-over of ingested fluid from the oesophagus into the trachea may easily occur and lead to asphyxia. Death due to this cause in premature infants often occurs following an attack of cyanosis during or immediately after a feed.

The lungs are deficient in elastic tissue and are slow to expand, so that pulmonary collapse occurs easily. The ingestion of fluid may lead to abdominal distension, and this results in an elevation of the diaphragm and a further tendency to pulmonary collapse.

Time of First Feeding

For these reasons delaying the initial feeding from the customary 24 hours after birth to 70 hours or more would seem a logical procedure if it did no harm to the infant.

During the past two and a half years this principle has been applied to 231 premature infants. The time of initial feeding has been in every case determined by the infant himself or herself. The routine is to place the infant in a cot immediately after his airway has been cleared, maintain an equable temperature (varying from 75 to 85° F. (23.9 to 29.4° C.) according to weight) and an adequate humidity (65%), and administer oxygen as necessary. The infant is kept as quiet as possible and away from bright light. The position in the cot is changed three-hourly and a fresh napkin applied when the previous one is soiled or wet. Recently some of these infants have been nursed naked and they have proved more active, so that routine three-hourly position-changing becomes less important.

After a variable number of hours the infant begins to cry—feebly at first and readily ceasing when his position is changed—but gradually the cry increases in strength and persistence and sucking movements of the lips are evident. When this occurs the first feeding is given. Table I shows the hour at which this happened. By this time the shock of birth and the effects of any maternal anaesthetic have passed and the increasing crying has led to some further expansion of the lungs.

TABLE I.—*Hour at Which First Feed was Given in 231 Cases*

Weight in lb. and oz.	No.	Hour of First Feeding		
		Max.	Min.	Average
2–2,7 (0·9–1·1 kg.)	9	96	26	60
2,8–2,15 (1·13–1·33 kg.)	23	102	31	73
3–3,7 (1·36–1·56 kg.)	35	105	15	61
3,8–3,15 (1·58–1·78 kg.)	58	111	28	61
4–4,7 (1·8–2 kg.)	67	106	19	53
4,8–4,15 (2·04–2·24 kg.)	39	105	20	48

Effects of the Starvation Period

What have been the effects of this period of starvation? First, the weight loss, as might be expected, has been greater than in infants fed earlier. Table II shows the weight loss in the various groups. The interesting features are that the average loss is similar, irrespective of the birth weight. But when this loss is recorded as a percentage of the birth

TABLE II.—*Weight Loss of Premature Infants at Fourth Day After Birth in 219 Cases*

Weight in lb. and oz.	No.	Weight Loss in oz.		
		Max.	Min.	Average
2–2,7	7	7	4	5 (14%)
2,8–2,15	20	11	4	6 (14%)
3–3,7	32	10	0	6 (12%)
3,8–3,15	58	13	0	6 (10%)
4–4,7	66	14	0	6 (9%)
4,8–4,15	36	11	0	6 (8%)

weight a marked difference is evident, the smallest infants losing nearly twice as much as the largest—yet with no evident deleterious effect.

In a series of infants nursed during 1947, before this "starvation regime" was in use, the average weight loss for infants of similar weights was 2½ oz. (71 g.). It will be observed that in four of the groups no weight loss occurred in the "minimum" column. In each of the 3 lb.–3 lb. 7 oz. (1.36–1.56 kg.) and 3 lb. 8 oz.–3 lb. 15 oz. (1.58–1.78 kg.) groups there was only one infant who did not lose. Small infants were routinely fed by gavage, which entailed no energy loss on the part of the infant, and this probably explains the apparent anomaly, for the weight loss was recorded routinely on the fourth day—this having been found to be the commonest day at which the lowest level was reached.

Secondly, the weight gain has been greater by the end of the third week than in a series routine-fed. Table III

TABLE III.—*Weight Gain of Premature Infants at 22nd Day After Birth in 181 Cases*

Weight in lb. and oz.	No.	Weight Gain in oz.		
		Max.	Min.	Average
2–2,7	7	15	0	6
2,8–2,15	18	11	−1	5
3–3,7	32	17	−1	7
3,8–3,15	53	29	−1	7
4–4,7	52	20	−7	8
4,8–4,15	19	14	−1	6

shows the gains attained. They represent excess over the birth weight, so that for the total weight gained the initial loss must be added. There is no doubt that when these infants did begin to feed they were more active and hungry and fed better: particularly was this so in the case of those infants nursed naked. (The totals in Tables II and III are lower than that in Table I because of the death or discharge from hospital of some infants.)

Thirdly, oedema of greater or less degree, which is of common occurrence in premature infants, disappears more quickly if fluid is withheld. Of these 231 infants 9% had oedema, and in every case it had disappeared at the end of 48 hours. In no case was feeding begun till oedema had disappeared.

Fourthly, rise of temperature might have been expected if dehydration became pronounced, comparable to the "inanition fever of the newborn" in bigger infants. Approximately a quarter of the infants showed elevations to 100° F. (37.8° C.) shortly before being fed, the temperature falling to normal within 48 hours of feeding. In no case were any symptoms evident. Special watch was kept on kidney function, but no abnormality was detected. The urines showed no increased incidence of albuminuria, there was no cylinduria or excess deposit, and no elevation of blood urea was encountered. At necropsy no ill effects were observed in the kidneys (or, indeed, in any other organs) either macroscopically or microscopically. The blood sugars showed the usual variations met in the newborn period, with an initial fall in the hours immediately after birth, and a subsequent rise, even before feeding was begun. The figures varied from 10 to 95 mg. per 100 ml. No case presented signs of hypoglycaemia. All the infants were given vitamin K, and no signs of hypoprothrombinaemia developed, but the importance of administering this vitamin as a routine should be stressed in view of the prolonged withholding of milk.

Nursing

It is well known that the ultimate factor in minimizing the death rate in premature babies is not breast milk or incubators or humidified isolation cubicles, but good nursing. The two sisters in charge of the units where these babies were nursed were both experienced and their opinions on this regime are therefore pertinent. They agree in regarding it as an improvement on the older method of routine feeding at a given fixed hour, and think it of particular value in the smallest infants. Their main feeling, however, is one of confidence that the great "post-feeding asphyxia" problem has largely disappeared and they can now go off duty with equanimity, knowing that they will not find one or more of the infants missing when they return to duty—having died of asphyxia following a feed.

A corollary of this is that the average period of starvation could probably be increased. When in any doubt about how much longer an infant will go, the sister will quite often feed him eight to ten hours earlier than necessary so that she may herself give him the first feed, rather than leave this hazard to a less-experienced colleague on night duty.

It may be asked if any of these small infants might not cry or show signs of hunger and die of inanition in consequence. This is unlikely, for only three infants of the 231 became markedly dehydrated and needed parenteral fluid. If there is any doubt about the safety of continuing starvation the state of renal secretion may help. Urination becomes progressively less as the hours pass, and a dry napkin for 24 hours continuously usually denotes that the time for fluid administration is approaching.

In the case of premature infants born at home who have to be transferred to a "premature unit" in hospital, it is important that the non-deleterious effects of withholding fluids should be more widely known, and that these infants should be given nothing by mouth before their admission to hospital. This would result in a fall in the number of deaths due to asphyxia and inhalation bronchopneumonia.

Summary

Attention is drawn to the advantages of delaying the first feeding of premature newborn infants till three to four days after birth. It is a safe procedure and has given excellent results. The actual time of first feeding is determined by the individual infant and is decided by his cry and by progressive diminution of urinary excretion.

We are indebted to Sister Goode, of the Duchess of York Hospital for Babies, and Sister Aumonier, of St. Mary's Hospital, who had the nursing care of these premature infants, and to the staff of these two hospitals. We are also indebted to Professor A. G. Watkins and Dr. J. Jacobs, of Cardiff, who introduced to our notice the technique and advantages of nursing premature infants in the nude. Particularly would we mention our debt to Dr. Clement Smith, of Boston, U.S.A., who described the rationale and results of his "starvation regime" to us in 1947.

Between April 21 and May 22 Dr. Macdonald Critchley went on a lecture tour in Turkey as visiting professor in neurology to the University of Istanbul. He also delivered lectures in Athens and in Ankara under the auspices of the British Council.

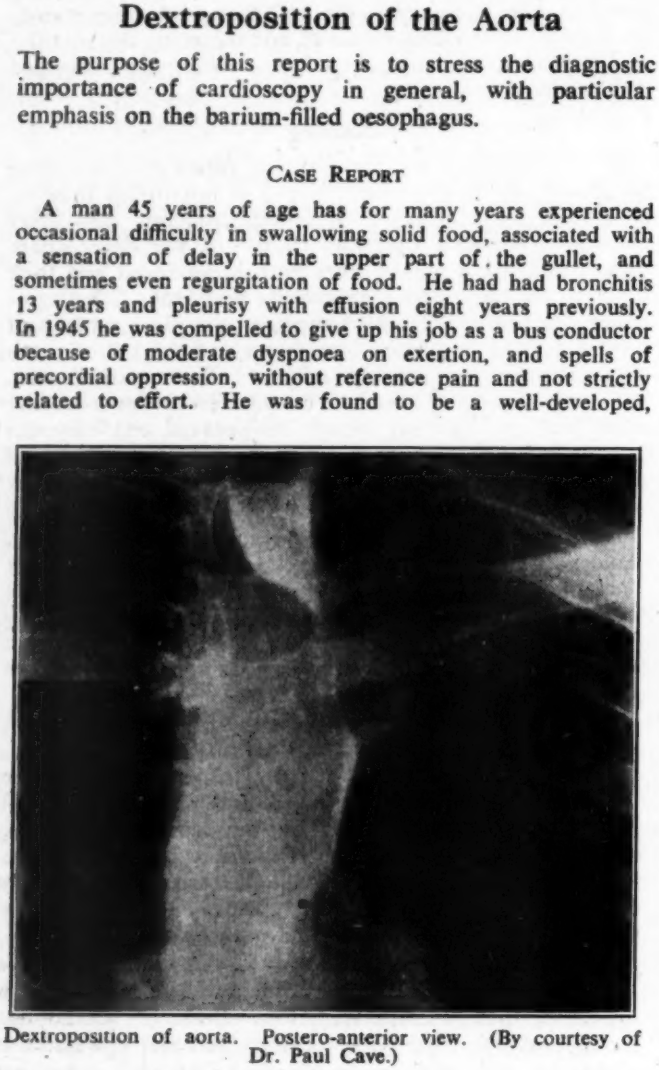
Medical Memoranda

Dextroposition of the Aorta

The purpose of this report is to stress the diagnostic importance of cardioscopy in general, with particular emphasis on the barium-filled oesophagus.

CASE REPORT

A man 45 years of age has for many years experienced occasional difficulty in swallowing solid food, associated with a sensation of delay in the upper part of the gullet, and sometimes even regurgitation of food. He had had bronchitis 13 years and pleurisy with effusion eight years previously. In 1945 he was compelled to give up his job as a bus conductor because of moderate dyspnoea on exertion, and spells of precordial oppression, without reference pain and not strictly related to effort. He was found to be a well-developed,



Dextroposition of aorta. Postero-anterior view. (By courtesy of Dr. Paul Cave.)

rather high-coloured man, with no sign of distress, dependent oedema, or clubbing. The brachial, femoral, and dorsalis pedis pulses were normal. Cardiac impulse was not perceived; the first apical sound was low-pitched; and the second basal sound to the right of the sternum markedly accentuated. Cardiac rhythm was regular; rate 64. Blood pressure in the right arm, in recumbency, was 140/105; in the left arm 135/105. Over both pulmonary bases there was diminished resonance on percussion, with scanty crepitation over the left base. Routine cardioscopy after barium swallow revealed a normal-sized heart silhouette, with a right-sided aortic arch.

The radiographic report (Dr. Paul Cave) read: "The aortic arch is small, but the vascular pedicle is slightly enlarged to the right of the midline. The descending thoracic aorta deviates to the right of the midline, but returns to its normal position just above the diaphragm. No abnormal pulsation was seen in the aorta. The oesophagus is compressed and displaced anteriorly and to the left of the midline in about three inches of its length from a level corresponding to the upper border of the clavicle. A smooth concave indentation is seen in the barium shadow on its posterior and right lateral aspects." (See illustration.)

The diagnosis of "right-sided aortic arch with persistence of the root of the obliterated left aortic arch, and left descending aorta" was made.

COMMENT

The essential feature of the dextroposition of the aorta is that the aortic arch crosses over the right main bronchus instead of over the left one. The right aortic arch is often associated with clinically and radiologically well-defined congenital malformations such as Fallot's tetralogy, isolated dextrocardia or dextrocardia within a complete transposition of all the viscera (situs viscerum inversus totalis), and coarctation of the aorta. It may be confused with the last-named on cardioscopy owing to the absence of the aortic knob in the normal position and to dilatation of the ascending aorta. But the evidence of high blood pressure in the upper extremities, weak or absent pulses in the leg arteries and the arterial collaterals of the trunk, scalloping of the ribs, and the familiar syndrome of coarctation is unmistakable. In Fallot's tetralogy the aorta overrides the interventricular septum, and so receives the blood from both the right and the left ventricle.

Aneurysmal dilatation of the ascending aorta is easily differentiated from the right aortic arch by studying the course of the oesophagus on barium swallow in the conventional positions. On the other hand, a right-sided aortic arch may be complicated with atherosclerosis, syphilis, or hypertension. The last-named seems to be the case in our patient.

The right aortic arch may occur in association with the following main vascular variations: (1) a left innominate artery arising as first brachiocephalic vessel from the aortic arch, the right common carotid as second, the right subclavian as third; (2) the left common carotid, the right common carotid, the right subclavian, and the left subclavian are given off the upper aspect of the aortic arch in that order; (3) a vascular ring formed by the pulmonary artery and a persistent ductus arteriosus or ligamentum arteriosum; (4) a persistent left aortic arch coursing anteriorly to the trachea, thus forming a double aortic arch.

In contradistinction to the right-sided aortic arch, the double aortic arch and vascular ring may sometimes give rise to a serious oesophageal and tracheal constriction calling for surgical relief. When such is the case there is no deviation of the oesophagus to the left, but constriction from right and left.

Finally, a vascular anomaly must be differentiated from the right-sided aortic arch—i.e., the anomalous right subclavian artery arising as the last branch from the left end of the normally placed aortic arch, and passing to the right behind the oesophagus. Rarely it gives rise to constriction of the oesophagus (dysphagia lusoria). The characteristic radiological signs can be elicited only upon a barium-filled oesophagus; there is just at the level of the upper margin of the aortic knob a small distinctly outlined semicircular deviation of the oesophagus to the right and ventrad; its intrinsic systolic pulsations have been observed in the antero-posterior view.

The differentiation of brachiocephalic vascular variations concomitant with a right-sided aortic arch in Fallot's tetralogy, or with a left aortic arch in dextrocardia complicated with cyanosis, is of practical importance to the surgeon who has to anastomose a suitable brachiocephalic vessel with the pulmonary artery (Blalock operation).

Only by combination of radiological and angiocardiographic methods of investigation can the topography of these vascular anomalies be identified.

I wish to express my thanks to Dr. E. Prideaux, Director-General of Medical Services, Ministry of Pensions, for permission to publish this paper.

EDMUND FINSTERBUSH, M.D., M.R.C.S.

Auricular Tachycardia Related to Phases of Respiration

There is no doubt about the frequent relationship between the cardiac and respiratory rhythms, though the correlating mechanism is not clear. Usually the relationship takes the form of sinus arrhythmia, but occasionally the result is more complicated.

Tisseuil (1932) describes four cases of a syndrome, associated with severe distress, occurring during the course of some other illness and consisting of paroxysms of cardio-respiratory synchronization on changing from the recumbent to the sitting position. In each case the synchronization consisted of a respiratory rate of 60 a minute with a pulse rate of 60, one cardiac beat occurring at the end of each inspiration, giving the observers the impression that the heart was locked with the respiratory rhythm. Miller and Perelman (1945) describe cases of auricular tachycardia related to changes of posture, without distress or notable changes in the respiratory rhythm.

In the following case auricular tachycardia occurred regularly on inspiration, with normal rhythm during expiration, and was accompanied by large synchronous changes in systolic blood pressure as a consequence of the periods of tachycardia.

CASE REPORT

A woman aged 55 was seen as an outpatient on June 28, 1949, complaining of shortness of breath on exertion for four months and palpitation of more recent onset. There was no paroxysmal or nocturnal dyspnoea and no pain. Some swelling of the ankles occurred, but not more than had been present for years. She was obese and had been gaining weight. An episode of irregular cardiac rhythm attributed to auricular fibrillation had recently occurred, and had disappeared after treatment with digitalis, phenobarbitone, and rest. The symptoms had improved at the same time. In 1923 *x*-ray treatment had been given for goitre.

On examination a moderate diffuse enlargement of the thyroid was noted, in front of which could be seen large dilated pulsating veins which did not empty when she sat upright. There was marked tremor of the outstretched hands. Her pulse rate was 130 and regular, blood pressure 210/105. Minimal nipping occurred at some arteriovenous crossings in the retinae. The heart sounds were normal. Radiography showed changes in the cardiac outline consistent with hypertension. Other systems were normal.

On admission ten days later, new and striking physical signs were discovered. Pulsus paradoxus was present, the radial pulse being hardly perceptible during normal inspiration. The systolic pressure was 180 during expiration and 120 during inspiration.

The electrocardiogram revealed the following: rate during expiration 88 a minute, during inspiration 183 a minute, the change in rate was always abrupt; the first complex in each period of tachycardia was premature and each period ended with a compensatory pause. Although the rate during inspiration is given as 183 a minute, it was not constant but started in each paroxysm at an average rate of 152, rising progressively to 187 and then falling to 165 just before the paroxysm ceased at the end of inspiration.

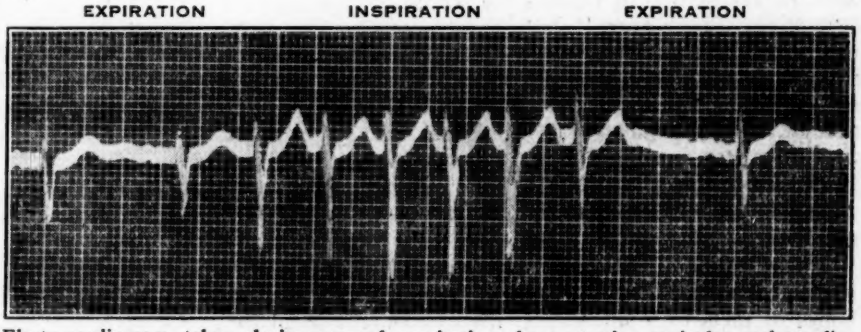
The ventricular complexes were normal. In parts of some tracings during the relatively slower phase of the tachycardia the P deflection was not hidden in the preceding T wave and the PR interval could be measured. It varied from 0.15 to 0.2 second, with an average of 0.17 second. The pacemaker was therefore in or near the sino-auricular node.

During an eleven-seconds period of holding the breath at the end of inspiration the electrocardiogram showed maintenance of normal rhythm. The rhythm remained normal during slow deep breathing. During voluntary rapid respiration the electrocardiogram showed normal rhythm for 19 seconds before tachycardia appeared.

The following tests were based on auscultation, which easily detected the changes of rhythm. Various normal and abnormal postures were induced without any effect on the regular appearance of inspiratory tachycardia. Similar negative results were obtained during pressure on each carotid sinus in turn and during moderate exertion insufficient to produce rapid respiration, which itself would temporarily abolish the dysrhythmia. The dysrhythmia was present on all of the fifteen occasions on which the patient was examined between July 8 and October 16, during which period she felt quite well apart from palpitation on more than moderate exertion.

The blood count and urine were normal. The Wassermann reaction was negative. The basal metabolic rate was 11%.

A course of quinidine, reaching a maximum daily dose of 25 gr. (1.6 g.), had no effect on the dysrhythmia. "Digoxin," 0.25 mg. twice daily for one month, was without effect. The initial dosage was sufficient to produce saturation. A three-months course of methyl thiouracil had no effect.



Electrocardiogram taken during normal respiration demonstrating auricular tachycardia occurring regularly during inspiration.

COMMENT

The abruptness of the changes, the rate, the prematurity of each first beat, and the compensatory pauses at the end of the periods place the tachycardia into the "paroxysmal" class. Two features which this dysrhythmia has in common with sinus arrhythmia are an increase of rate during inspiration and a normal rhythm while holding the breath. It is interesting to note that the rapid alternating changes in systolic pressure were symptomless.

Possible aetiological factors in this case were hypertension, arteriosclerosis, and old hyperthyroidism.

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The Ministry of Health states that blood donors set up a new post-war record in 1949 by contributing over 456,000 bottles of blood to the National Blood Transfusion Service for hospitals in England and Wales. This was an increase of 72,000 gifts on 1948 and of 160,000 on 1947. New donors totalled 133,000 compared with 98,000 and 72,000 in the two preceding years, but another 200,000 are needed to reinforce the 369,000 on donor panels at the end of the year.

Reviews

THE NORMAL FIGURE

Normal Values in Clinical Medicine. By F. William Sunderman, M.D., Ph.D., and Frederick Boerner, V.M.D. (Pp. 845; 237 figures. £3 10s.) Philadelphia and London: W. B. Saunders Company.

It is difficult to define the "normal" in clinical medicine, since the "norm" for healthy persons varies with age, sex, race, climate, diet, and other conditions. The purpose of this book is to "present a discussion and compilation of values which may be termed 'normal.'" There are 19 main sections on normal values in cardiology, haematology, the chemical components and physical properties of blood, the respiratory tract, the digestive system, neurology, urology, gynaecology and obstetrics, orthopaedics, dermatology, ophthalmology, otology, rhinology, endocrinology, metabolism and nutrition, and dentistry. Finally there are articles on anatomical normals, statistical methods, food values, drugs and their doses, isotopes, life and actuarial tables, weights, measures, and standards.

How often do we ask ourselves when conducting a clinical examination or reading the laboratory reports on a case, What are the normal findings or figures? This book will supply the answers. We must remember, however, that the normal figures for laboratory tests may vary. It is a little bewildering to the physician, accustomed to the accuracy of his clinical observations, to find, for example, that the normal maximum blood uric acid figure is 4 mg. per 100 ml., and a year or so later, owing perhaps to a change in the laboratory staff, to be told that the figure has now fallen to 2.5 mg. per 100 ml.

This is essentially a book for reference, but each section is full of interest and the writers have covered the bare bones of facts with sinews and flesh and made them live. Some, perhaps, may think the book is too long; but, as Montaigne wrote, "Every abridgment of a good book is a foolish abridgment," and this is undoubtedly a very good book and one I would like to possess.

G. E. BEAUMONT.

MEN IN THE SUN

Tropical Fatigue. By R. K. Macpherson, M.Sc., M.D., University of Queensland Papers, Department of Physiology. Volume 1, 1949, No. 10. (Pp. 162. 17s. 6d.) Brisbane: University of Queensland Press. 1949.

A field investigation into the nature and incidence of tropical fatigue, sponsored jointly by the Australian Army physiological research committee and the flying personnel research committee of the Royal Australian Air Force, was carried out under Dr. Macpherson's direction in 1944–5. A long-term inquiry was planned, but it was brought to a close by the collapse of Japan, which occurred soon after the completion of the preliminary survey. The subjects examined were R.A.A.F. and R.N.Z.A.F. ground crews and A.I.F. soldiers serving in the Netherlands East Indies, New Guinea, and the Solomon Islands. In all, 1,807 men were examined, including a control group of 251 stationed in a non-tropical climate on the mainland of Australia.

The problem was to determine whether such a condition as tropical fatigue in fact existed; and, if so, whether its nature was physical, mental, or a combination of both. The physical examination included an assessment of cardiovascular stability by the use of a tilt-table and by recording resting pulse rates and blood pressures; determination of physical fitness by the Harvard pack test; measurement of sweat loss and sweat evaporation; and performance of a moderate exercise test.

Belief in tropical deterioration was widely prevalent among the subjects studied, and the observations and inquiries of the author convinced him that such deterioration really existed. Beyond a slight initial decrease in weight, however, and a doubtful increase in vasomotor instability, the only evidence of physical deterioration was that given by the Harvard pack test index, which showed a net fall of 0.19 unit per week of tropical service. The degree of physical deterioration was insufficient to account for the marked loss of efficiency, and it was concluded that a large part of the deterioration was of a psychological nature. It was difficult to determine how much of this psychological deterioration was directly attributable to extremes of temperature and humidity and how much was due to other factors, such as boredom, isolation, the conditions of service generally, and to the mental inadequacy or psychological insufficiency of the men themselves; but the conclusion was reached that climatic conditions played a major part.

The author points out that his observations relate only to healthy young adult males exposed to a tropical climate for a short period. He stresses the need for obtaining information on the effect of long-term exposure, not only on healthy young men, but also on the infant, the aged, and the child-bearing woman.

G. COVELL.

TOXIC HAZARDS IN INDUSTRY

Industrial Toxicology. By Lawrence T. Fairhall. (Pp. 483. £2 6s. 6d.) London: Baillière, Tindall and Cox. 1949.

In spite of the ever widening scope of occupational medicine, industrial toxicology is still an important subject. With the increasing interest in the many social and occupational factors affecting the health of the worker, toxicology has been regarded as less important, and indeed the toxic episodes occurring in industry are looked upon as museum pieces, as events which in the sum total cause only a small fraction of industrial sickness and fatalities. Statistically this may be true, and this truth has been emphasized by the many medical officers who are now responsible for the health of industrial communities in which there are few or negligible toxic hazards. But unlike many conditions, such as duodenal ulcer or coronary disease, which are now thought in some instances to be occupational diseases, the cause of industrial poisoning is indisputable and it can be prevented. Industrial medical officers cannot do much to prevent the stresses and strains of work life, but they will always be expected to reduce the toxic hazards to a safe minimum—thus they (and other technical experts in industry) must be aware of the degree of toxicity of substances which are used in their industries. The constant change of processes makes this a difficult task. This is not only the result of ignorance of the behaviour of substances: there are few up-to-date textbooks which give briefly and simply an outline of the toxicity of substances widely used and well known, as well as the new and less familiar poisons which are constantly being introduced.

The purpose of this book is "to serve as a bridge between the rapidly expanding field of toxicological investigation

and the application of this knowledge of industrial poisons by the industrial hygienist." It is not a complete manual on industrial toxicology—it would be too voluminous and unreadable if it were—but there are a few important omissions. There is little mention of the industrial cancers, and therefore no reference to the carcinogenic properties of arsenic, nickel carbonyl, the tar products, and mineral oil. Nevertheless, the book may prove to be one of the most useful manuals of industrial toxicology yet written. It is concise and readable, with good references which are by no means confined to investigations carried out in the U.S.A.

The text is in two parts, on inorganic substances and on carbon compounds, with an excellent introductory chapter on toxicology. Each substance is discussed under the headings of characteristics, industrial uses, toxicity, and analysis. It is written primarily for industrial hygienists, that is to say that invaluable body of men who by their training may be physicists, chemists, or engineers, but who are responsible for assessing a hazard and eliminating it. It will be invaluable to industrial medical officers also They may be the first to recognize a hazard or to be asked, particularly in Great Britain, about the toxic properties of materials in use or about to be used. It can be strongly recommended to the medical student and doctor.

R. S. F. SCHILLING.

FUNDAMENTALS OF ELECTROCARDIOGRAPHY

Electrocardiography. By Louis Wolff, M.D. (Pp. 187; illustrated. £1 2s. 6d.) Philadelphia and London: W. B. Saunders Company. 1950.

This book is unusual in that it does not attempt a complete survey of electrocardiographic abnormalities. Only those which affect the ventricular complex are considered, and no mention is made of the auricular arrhythmias. The reader is given a short but admirable account of dipoles, depolarization, repolarization, vectors, the mean electrical axis, and so on to the ventricular gradient and primary and secondary T-wave changes. A discussion follows, based on these principles, upon the reasons for the curves obtained with standard and unipolar precordial and limb leads in bundle branch block, ventricular hypertrophy, and cardiac infarction.

Since the book is founded on lectures, the presentation is dogmatic and little account is given of opposing views This leads to difficulties, such as in the statement made on page 62 and illustrated on page 63, that in right ventricular hypertrophy a deep S wave in lead aVL signifies a horizontal position of the heart. Few cardiologists would agree with this, nor does it accord with the interpretation of Fig. 53 given on page 121, which follows the conventional view that this denotes a vertical position. The importance in horizontal hearts of the negative zone behind the impulse as it spreads through the wall of the left ventricle, stressed by Goldberger, is not mentioned.

The second part of the book contains cardiograms with short case histories illustrative of the different conditions under discussion. There is also included a well-balanced account of the use and limitations of cardiograms in the diagnosis of ventricular myocardial disease. The book can be recommended to all those who desire to become conversant with the principles on which modern cardiography is based.

CURTIS BAIN

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Biochemical Aspects of Genetics. Biochemical Society Symposia No. 4. Organized and edited by R. T. Williams. (Pp. 60. 6s.) Cambridge: University Press. 1950.

Schistosomiasis in South Central Africa. By M. Gelfand, M.D., M.R.C.P. (Pp. 239. 25s.) London: H. K. Lewis. 1950.

Modern Practice in Dermatology, 1950. Edited by G. B. Mitchell-Heggs, O.B.E., M.D., F.R.C.P. (Pp. 836. 63s., postage 1s. 6d.) London: Butterworth. 1950.

Quinidine in Disorders of the Heart. By H. Gold, M.D. (Pp. 115. 16s.) London: Cassell. 1950.

Ask the Children. By F. Thomson, M.B., I.M.S. (Pp. 288. 15s.) London: Cassell. 1950.

Directory of Convalescent Homes Serving the London Area, 1950. (Pp. 183. 7s. 6d.) London: King Edward's Hospital Fund. 1950.

Notes on Communicable Diseases of Laboratory Animals. By H. J. Parish, M.D. (Pp. 69. 3s.) Edinburgh: Livingstone. 1950.

Industrial Health. By R. Passmore, D.M., F.R.S.E., and C. N. Swanston, D.P.H., D.I.H. Foreword by F. A. E. Crew, F.R.S. (Pp. 110. 4s 6d.) Edinburgh: Livingstone. 1950.

Freud or Jung. By E. Glover. (Pp. 207. 15s.) London: George Allen and Unwin. 1950.

Water and Salt Depletion. By H. L. Marriott, C.B.E., M.D., F.R.C.P. (Pp. 80. 15s.) Oxford: Blackwell Scientific Publications. 1950.

Cold Spring Harbor Symposia on Quantitative Biology. Amino Acids and Proteins. Vol. 14. (Pp. 217. $7.00.) Cold Spring Harbor, L.I., New York: The Biological Laboratory. 1950.

The Nose. By T. H. Holmes, M.D., and others. Foreword by W. T. Longcope, M.D. (Pp. 154. 32s. 6d.) Oxford: Blackwell Scientific Publications.

Histology. By A. W. Ham, M.B. (Pp. 756. 80s.) Philadelphia, London, and Montreal: Lippincott. 1950.

Über die Behandlung der Angeborenen Hüftgelenksverrenkung. By G. Ihlenfeldt. (Pp. 66. M. 6.00.) München-Berlin: Urban and Schwarzenberg. 1950.

Les Radiesthesistes devant l'Opinion Publique. By G. Jacquemyns. (Pp. 55. No price.) Brussels: Institut Universitaire d'Information Sociale et Economique. 1950.

Klinik der Zahn- Mund- und Kiefer-Krankheiten. By H. Wolf. (Pp. 222. M. 16.00.) München-Berlin: Urban and Schwarzenberg. 1950.

Human Fertility and Problems of the Male. By E. J. Farris, Ph.D. (Pp. 211. No price.) New York: The Author's Press. 1950.

La Dermatologie aux Etats-Unis d'Amérique. By L. van Lierde. Preface by C. Simon. (Pp. 72. 50 Belgian francs.) Brussels: Acta Medica Belgica. 1950.

Die Chirurgie der Schilddrüse. By W. Gattig. (Pp. 96. M. 5.50.) Halle (Saale): Carl Marhold. 1950.

La Schermografia di Massa nella Diagnosi Precoce delle Malattie Sociali. By S. Collari. (Pp. 206. No price.) Rome: Istituto di Medicina Sociale. 1950.

Le Guide Thérapeutique du Medecin Praticien. By J. Trabaud. Vol. 9. *Les Maladies des Yeux, des Oreilles et de la Peau.* Preface by Tanon. 2nd ed. (Pp. 375. No price.) Paris: Vigot. 1950.

Lehrbuch der Anatomie des Menschen. By A. Benninghoff. 3rd ed. Vol. 3. (Pp. 415. M. 30.00.) Berlin-München: Urban and Schwarzenberg. 1950.

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THE GENERAL ADAPTATION SYNDROME

Recently, in one of our contemporaries, an anonymous reviewer remarked that it was unfortunate that so far endocrinologists had made no attempt to integrate their subject with the body of general medicine. By those endocrinologists who believe that their science is the main integrating influence in medicine the remark was greeted with some surprise. It was clear that more than 13 years after the first publication of Hans Selye's work[1] a presumably eminent reviewer had not yet heard of it. Until the summer of 1949 his ignorance was shared by the majority of the medical profession. Even the publication in 1946 of his monograph[2] on the general adaptation syndrome caused no stir, and indeed provoked something rather like scepticism from some of the few who read it. Then in 1949 the application of his work to the treatment of rheumatoid arthritis suddenly changed neglect into enthusiasm.

The foundations of medicine are often hard to seek. Selye himself, in the paper published in the opening pages of this issue, mentions Claude Bernard as one of those who laid them, with his concept of the constancy of the internal environment. But it is to Selye that we should ascribe not only the fundamental work but most of the superstructure of the building which he has called the "general adaptation syndrome," the very existence of which remained unobserved by many until the decorators got to work, notably at the Mayo Clinic, but also in many other hospitals in many countries of the world. "Anything which causes stress endangers life unless it is met by adequate adaptive responses." It has always been assumed that each stress calls forth a specific response: a fall in temperature stimulates the thyroid gland, a reduced blood sugar calls forth an increased secretion of adrenaline, fear activates the adrenal medulla. It was not previously realized that in addition to a multitude of specific responses there existed a general response, a call to arms of the whole adaptive process of the body, unspecific in its form, occurring in answer to any and every form of attack from without or even perhaps from within. Such attacks need not be more than potentially lethal, and indeed many apparently innocuous stimuli may activate what Selye called the "alarm reaction"—for example, a rise or fall in temperature, a fall in atmospheric pressure, or even severe muscular activity. It follows that the general adaptation syndrome never occurs in a pure form. The response to stress must always be a mixture of the specific response with the unspecific response. These specific responses thus act as "conditioning factors" in the general pattern of response, perhaps reducing one part or increasing another, or even adding new signs or symptoms which are no part of the general syndrome. Other circumstances may still further complicate the issue, especially heredity, pre-existent disease, and the effects of diet, on which Selye has laid special emphasis.

The measures of defence called forth by stress are co-ordinated by the hypothalamus and both lobes of the pituitary gland. They are therefore in part autonomic and in part endocrine. How these headquarters are brought into action is still unknown. The message may reach them from the threatened area by nervous or by humoral means or by both. The autonomic responses have long been recognized by physiologists, but the endocrine responses are only now beginning to become clearer. The principal one is a "shift" in pituitary activity. Selye suggests that the anterior lobe is incapable of discharging all its hormones together to a maximum degree. The one most necessary for the preservation of life is corticotrophin—which recent recruits to endocrinology prefer to call A.C.T.H.—and this is produced in increased quantity. On the contrary, the output of gonadotrophins, thyrotrophin, and somatotrophin is reduced. The increased output of corticotrophin induces the adrenal cortex to increase its output of gluco-corticoids, including the hormone which has recently sprung into fame as cortisone. These act upon the blood, causing lymphopenia, eosinopenia, polymorphonuclear leucocytosis, a fall in the erythrocyte sedimentation rate, decreased clotting time, and accelerated fibrin formation; on the lymphatic tissue, causing atrophy especially of the thymus; on the reticulo-endothelial system, with an increase in phagocytosis and antibody formation; and on sugar metabolism, causing an increased transformation of protein into sugar. In addition the gluco-corticoids have a slight mineralo-corticoid activity and bring about in a minor degree the changes associated with the administration of desoxycorticosterone. Nevertheless, in general, the gluco-corticoids and mineralo-corticoids antagonize each other.

Selye has divided the general adaptation syndrome into three parts: the alarm reaction or call to arms; the stage of resistance, in which the enemy is held; and, if he does not retreat (if, that is, the stress continues),

[1] *Brit. J. exp. Path.*, 1936, **17**, 234.
[2] *J. clin. Endocrinol.*, 1946, **6**, 117.
[3] *Endocr. Sci. Contit.*, 1946, **18**, 189.
[4] *Proc. Mayo Clin.*, 1949, **24**, 181.
[5] *British Medical Journal*, 1950, **1**, 1362.

the ultimate defeat or stage of exhaustion, in which many of the changes of the alarm reaction, which have disappeared during the stage of resistance, again make their appearance as a prelude to death. It might be expected that, just as an aberration of other physiological mechanisms is a cause of disease, so diseases would arise from aberrations of the mechanism of defence. Such diseases have gradually become recognized in the last 14 years. In one of his earlier papers Selye himself suggested that the arteriosclerotic and rheumatic groups of diseases were examples of the adaptation syndrome "going off the rails," and later he produced arthritis in animals by treatment with excessive doses of desoxycorticosterone combined with a high salt diet. It was only one mental step to the hypothesis that corticotrophin or the gluco-corticoids might undo what the mineralo-corticoids could do, but work along such lines was hampered by the war and, when the war was over, by shortage of materials. Nevertheless work went on in several countries. In 1946 Bassi and Bassi[3] of Bologna, for example, successfully treated rheumatoid arthritis with an adrenal extract. The isolation by Kendall in 1941 of "compound E" and its recent large-scale production under the name of cortisone gave to the workers at the Mayo Clinic an opportunity which they were quick to seize. The astonishing results of Hench[4] and his colleagues brought the work of Selye from the laboratory and the study into the ward and, it is to be feared, into the market-place. They gave to Selye's work a practical bent which he acknowledged with characteristic generosity in his recent lecture.[5]

The American workers have stressed that the control of rheumatoid arthritis is not easy and will not be so until far more is known of the mechanism of its beginnings, the mode of action of cortisone, and the conditioning factors. There are snags to be overcome, especially the unfortunate fact that unless due care is exercised the patient may surrender his arthritis only in return for Cushing's syndrome or diabetes mellitus. Moreover, rheumatoid arthritis is only one disorder of adaptation. Selye's suspicion descended early not only on this disorder but on periarteritis nodosa, essential hypertension, nephrosclerosis, acute nephritis, rheumatic fever, allergy, certain types of diabetes, and perhaps some cases of thyrotoxicosis. Even before Selye, peptic ulcer was known to be associated sometimes with such widely different predisposing causes as mental trauma, wound shock, burns, and frostbite. To these he and others have added the astonishing list which appears in his paper in our present issue, a list which includes not only the diseases in which A.C.T.H. and cortisone have helped, or theoretically might help, the patient, but those in which they have, or might have, deleterious effects, because the derailment of the defence mechanism is on the other side of the track.

Selye's hypothesis is a startling one and for this reason alone it will not gain immediate universal acceptance. Many of the criticisms which spring to the mind are dealt with in this paper. Many more will arise and some of them will prove just. Parts of the building will from time to time prove unsound. New rooms will be added and old rooms will have new decorations. As Selye himself said in his Heberden Oration, facts must be true, but a theory need not be entirely true. The value of a theory lies in its capacity to weld together isolated facts into a whole greater than the sum of those facts, and in its capacity to stimulate research. No theory in living memory has possessed these virtues to a greater extent than that of the general adaptation syndrome, and no development from it, however great its practical significance, can detract from the credit which belongs by right to its originator, whose Heberden Oration on June 2 and 3 will long be remembered by those who were present: the occasion was marked by the presentation to Professor Selye of the Heberden medal.

SMALLPOX AND PUBLIC HEALTH

The recent outbreak of variola major in western Scotland demonstrates the ease with which infection can enter the country despite strict precautions at seaports and airports, the difficulty of distinguishing from varicella modified variola occurring in a person who retains a partial immunity as a result of earlier vaccination, the continuing necessity for infant vaccination, and the great importance of maintaining an efficient public health service. Laidlaw and Horne[1] have now told the story of the outbreak in some detail. The s.s. *Chitral* sailed from Bombay on February 11, called at the smallpox-free ports of Aden (February 16) and Port Said (February 20–22), and docked at the Port of London on March 5. Whether there had been a missed case on board is a matter of speculation, but when the ship reached Britain there was certainly no evidence of the presence of smallpox. After travelling by train to Glasgow an Asian seaman from the *Chitral* developed pneumonia (diagnosed clinically and radiologically) and was admitted to an infectious-disease hospital in the city on March 10. Four days later, without having had any recurrence of pyrexia, he developed a papulo-vesicular rash which was regarded as varicella by experienced consultants who were aware that he had recently come from India. The patient was transferred to an isolation ward, and discharged as cured on March 23. His contacts while in hospital included the staff and patients of two wards, visitors to these wards, a class of undergraduates, and a class of postgraduate students. On March 26 smallpox was diagnosed among

[1] *Med. Offr*, 1950, **83**, 187.

these contacts. Six cases were removed to a smallpox hospital on that day—three from the original hospital, two from other hospitals to which they had been admitted, and one from the patient's own home—and by March 31 there had been transferred to the smallpox hospital the original patient and 20 contacts, of whom 17 definitely had smallpox. Two of the remaining three were found not to be suffering from the disease, and the diagnosis in one case remains doubtful. Many of these patients had numerous contacts.

The usual measures of control—contact tracing, vaccination of contacts, surveillance, etc.—were promptly applied, though contact tracing was difficult. For example, the medical students were already on vacation, and five of them had left no address. Surveillance, which meant the daily visiting of some 2,000 persons in Glasgow alone, also led to much correspondence with other medical officers of health, especially as the period of surveillance included the Easter week-end. After general practitioners had been invited to seek the advice of the public health staff in cases of doubt medical officers of the Glasgow health department were called upon to examine over 800 patients. Simultaneously there arose, not unnaturally, a considerable public demand for vaccination in the city, and 162,000 persons were vaccinated at centres opened by the public health department, while 220,000 doses of lymph were supplied to general practitioners. Despite the great number of contacts not a single tertiary case occurred. Though the danger of spread was greatest in Glasgow, much work had to be undertaken by doctors in other towns and districts outside the city. In Hamilton, home town of one of the patients, contacts were so numerous that it was hopeless for a small public health staff to attempt to employ the standard measures of control, and the medical officer of health found it necessary to introduce mass vaccination. Local practitioners co-operated to the full, and practically every person in the borough was vaccinated. In many Scottish and some English counties and towns medical officers of health had to trace and observe contacts. Last, but not least, a heavy burden of responsibility must have fallen on the shoulders of the medical officers of the Department of Health for Scotland.

Of the 18 confirmed cases 6 had no vaccination scars. These 6 patients all died and were the only patients to die. Of the 12 (or 13 if the doubtful case is included) with vaccination scars, all save two had smallpox in modified form; the two who had more severe attacks had both been successfully vaccinated once—18 and 43 years ago respectively. Apart from the doubtful case (revaccinated in 1946) none of the patients had been successfully vaccinated or revaccinated within the last seven years. The history of the primary case in this outbreak reveals how easily smallpox can enter the country in these days of speedy travel. Airport sanitary services, however excellent, cannot prevent the subsequent appearance of smallpox in a person who reaches Britain apparently well but actually in the early stage of incubation. Hence it becomes plain that vaccination of infants is at least as necessary as ever before, and that persons who may encounter the disease—e.g., staffs of isolation hospitals—should be periodically revaccinated. The value of vaccination is well demonstrated by the fact that all the fatal cases were in persons without vaccination scars and by the fact that no confirmed case occurred in any person who had been successfully vaccinated within the previous seven years. "It is of fundamental importance," write Laidlaw and Horne, "to sustain an efficient public health service of knowledgeable and experienced medical officers, a service still available but threatened with extinction due to failure to recognize preventive medicine as an indispensable element in an integrated National Health Service." This is one of the important lessons of the recent outbreak. It was greatly to the credit of the public health services, local and central, that the outbreak was rapidly suppressed and an epidemic prevented, for the medical staff was below strength. Service in central Government Departments and with local authorities must be made sufficiently attractive to induce able young doctors to train for a career in preventive medicine. When these services are further weakened by retirement of some of the older men it is quite possible that the country may have to face the dangers and expense of a major epidemic—with all the industrial and economic disruption that such a catastrophe causes—because the staffs of public health departments have become too weak to limit the spread of what should have been merely a localized outbreak.

ILLNESS IN INFANCY

In some ways infant morbidity, though much more difficult to put into figures and to record accurately because of diagnostic difficulties, is a better guide to the health of a community than infant mortality, which varies with the size of family, age of the mother, and spacing of births. Studies of the relationship of infant morbidity and mortality to social factors can provide useful information, and Dr. R. M. Dykes, medical officer of health for Luton, has recently published a valuable report on the sickness experience of infants born in Luton in 1945.[1] The figures revealed the unexpected fact that while there was the usual gradient for infant mortality according to social class (31 per 1,000 in social classes 1 to 3 and 52 per 1,000 in classes 4 and 5, with an overall mortality of 36), no such gradient was apparent for infant morbidity. More than half the total sickness was concentrated in less than 7% of the infants, and those 7% were evenly distributed through the social classes. The reason for this was not

[1] *Illness in Infancy*, 1950, Luton.
[2] *J. Pediat.*, 1949, **35**, 43.

clear, and the same finding would not necessarily be made in other towns. Dr. Dykes suggests that whereas the differences between the social classes were apparently without effect on sickness incidence, they do play a part in determining the risk of death when an infant becomes sick. It may be that the sick infant in the lower social classes receives less care than his fellow in the upper social classes, or that medical attention for the upper classes is better and sought earlier than it is in the lower. Again, though the resistance to infection may be no different in the various social classes, the resistance to disease once acquired is perhaps greater in the upper classes than in the lower. One of the reasons for the establishment of the National Health Service was to sever the connexion between economics and health, and it is to be hoped that Dr. Dykes will prepare further reports to show whether the differences observable in the 1945 figures persist from year to year or tend to disappear. The Luton figures also showed that the incidence of illness increases with family size, and that there was more sickness among artificially fed babies than breast-fed ones, largely because of the high incidence of gastro-enteritis in the former. In the Luton series gastro-enteritis accounted for 11% of illnesses; in Rochester, Minnesota, where Norval and Kennedy[2] have recently studied the amount of illness among infants in the first year of life, the corresponding figure was 19%. It is to be hoped that other public health authorities will follow the lead given by Luton in making full use of the mass of data concerning morbidity which is available to them.

THE LADY TATA MEMORIAL TRUST

In 1932 Sir Dorabji Jamseti Tata, of Bombay, founded the Lady Tata Memorial Trust to commemorate his wife, the late Lady Tata, C.B.E. Four-fifths of the Trust income has since been devoted to subsidizing research on diseases of the blood, and particularly leukaemia. Elsewhere in this issue we publish the names of those who are to receive awards for research during the year beginning October 1, 1950. The European Scientific Advisory Committee of the Trust has recently published a report on the working of the Trust from 1933 to 1947. The Committee, in recommending grants from the Trust funds, has assumed that little further progress would come from purely clinical inquiries. The bulk of the research has, therefore, been concerned with spontaneous and experimental leukaemia in animals. Most of this work has been done in three centres—New York, Paris, and Copenhagen. Professor Furth's studies of mouse leukaemia, extending over the period 1935–46, are well known. The late Professor Roussy at the Institut du Cancer in Paris investigated spontaneous transmissible and induced leukaemias in fowls and rats, and in Copenhagen Professor Engelbreth-Holm has studied the problems of leukaemia in fowls and mice; he is the author of a valuable monograph on spontaneous and experimental leukaemia in animals. The main facts concerning the leukaemia of animals have been established largely with the generous financial aid of the Lady Tata Memorial Trust. It has been shown that mammalian and human leukaemia are comparable, and a solid foundation has been laid on which we may hope to see erected structures of help to the physician in his struggle with the disease in man.

[1] *Report on the Working of Lady Tata Memorial Trust (International Section) from 1933 to 1947*, 1949, Bombay.

NEW SUBSTANCE IN TUBERCLE BACILLI

The tubercle bacillus has been fractionated chemically on a scale unsurpassed by similar efforts with any other micro-organism. Its main constituents—lipoid, polysaccharide, and protein—are well known, and their separate effects in living tissue have been carefully studied.[1] It is thus a little surprising as well as stimulating to read that another constituent, evidently of importance in pathogenicity, has been demonstrated and extracted by quite simple means. The work takes its origin from studies of colonial morphology in *Myco. tuberculosis* by Dubos and Middlebrook, who found that the formation of long "cords," as distinct from mere clumps, was associated with virulence. They suspected that a chemical factor might be responsible for this characteristic aggregation as well as, perhaps, for other properties of virulent bacilli, and it is this factor which has been studied by Bloch.[2] He found that if cords of such bacilli were brought into contact with paraffin oil they could be seen to be disrupted, only scattered individual bacilli being left: this strongly suggested that something had been removed which held them in their parallel arrangement. Lighter solvents of this series had an even more rapid effect, and petroleum ether was used for extracting wet bacilli in an attempt to isolate the substance concerned. It is of some interest that dried organisms do not yield it, apparently because the substance is soluble in mineral oil only in the presence of water. A small yield was obtained of an amorphous colourless material, lipoid in nature, acid-fast but quite distinct from mycolic acid: it could be obtained only from young cultures of virulent bacilli, not from avirulent organisms. It was proved by ingenious means to have the same action in immobilizing leucocytes as that possessed by virulent tubercle bacilli and recently demonstrated by Bloch himself.[3] This was achieved by coating *B. subtilis* with the substance, which then behaved like virulent *Myco. tuberculosis* in preventing leucocytic migration *in vitro*. The substance was toxic to mice, but only after repeated injections, and the shortest interval before death occurred was never less than nine days. Extracts of other *Mycobacteria* prepared in the same way had little or no action in preventing leucocytic migration, but some of these and a similar extract of mammalian tissue were toxic to mice, evidently in some non-specific way. The substance had no tuberculin activity. The behaviour of tubercle bacilli from which it had been extracted is interesting. That they were not killed was proved by viable counts of extracted and unextracted bacilli. On the other hand, animals inoculated with them survived much longer than controls, and some showed no gross lesions at all after long periods. It seems that tubercle bacilli deprived of the "cord factor," although unimpaired in viability, are lacking in pathogenicity until the substance has been

[1] Sabin, F. R., *Amer. Rev. Tuberc.*, 1941, **44**, 415.
[2] *J. exp. Med.*, 1950, **91**, 197.
[3] *Amer. Rev. Tuberc.*, 1948, **58**, 662.

reformed and are unprotected against phagocytosis: hence a large but variable proportion is destroyed before lesions can be produced.

It is tempting to compare the cord factor of tubercle bacilli with the capsular polysaccharide of the pneumococcus: both are surface substances, protective to the organism, and hence necessary to pathogenic activity. It remains to be determined whether the substance extracted by Bloch is pure or a mixture of different lipoids, and hence whether it is itself acid-fast or whether its acid-fastness in his hands is due to an admixture of mycolic acid. The failure to recognize its separate existence before can be explained, as he says, by the fact that previous extractions have usually been carried out with dried bacilli, from which it cannot be removed: it also forms so relatively small a fraction (the yield being 1 part in 2,000 or less of total bacillary weight) that its presence among lipoids obtained by other methods could have been overlooked. The evidence seems strong that this hitherto unrecognized substance plays a vital part in the tuberculous process.

MOTOR-CYCLE ACCIDENTS

From experience at the Military Hospital for Head Injuries at Oxford, where 70 out of the first 290 patients with blunt head injury during 1940 were motor-cyclists, Sir Hugh Cairns was led to report in the following year[1] on the comparative mildness of symptoms in those—only 1 in 20 at the time—who had been wearing crash-helmets. In November, 1941, the Army Council made crash-helmets compulsory for motor-cyclists. Later, Cairns and Holbourn[2] showed that the incidence of fractured skulls was reduced to one-quarter by the pulp helmet, and such fractures as occurred were less severe. Cairns's demonstration is described as "conclusive" in an analysis of 579 accidents to Army motor-cyclists carried out by Major D. F. Bayly Pike, officer-in-charge of the traffic accident section of the Army Operational Research Group, and recently published by the Department of Scientific and Industrial Research.[3] Of the 579 accidents investigated, 16 were fatal, 167 serious, and 396 slight. In each of the 16 fatal cases the accident accounts refer to "head-on crashes" and to "instantaneous death," and it is recorded that eight of the machines were sold as scrap metal and the other eight "repaired only at great expense—front wheels, front forks, and main frames being replaced in most cases." If the machine had to be damaged to that extent before the rider was killed it would seem that the regulation crash-helmet had succeeded in setting a very reasonable standard for fatality. In the 106 "serious" accidents on which medical reports were available 29 of the riders suffered from concussion, and it is considered that many of these might have died but for the crash-helmet. An unexpected fact brought out in an analysis of manœuvres leading to accidents is that in 238 out of 579 cases no other vehicle but the motor-cycle was involved. By far the commonest manœuvre to cause accidents was a right-handed turn by another vehicle with the motor-cycle overtaking: the reason for this is that there is a large area behind a car or lorry in which a motor-cyclist is quite unable to see the signals made by the driver with either his hand or a "trafficator." This was also the manœuvre found to be most common in an investigation in Oxfordshire of road accidents of all types. The other manœuvres leading to accidents in order of frequency were: a straightforward cross-roads collision; normal passing, with the vehicles proceeding in opposite directions; and a right-hand turn by another vehicle with the motor-cycle advancing towards it. Because of the frequency of leg injuries (predominant in both serious and slight cases) investigation is suggested into the efficacy of the various forms of leg protection that could be provided. There is also a recommendation that physiological research should be undertaken to throw light on the ability to detect changes in speed and distance.

[1] *British Medical Journal*, 1941, **2**, 465.
[2] Ibid., 1943, **1**, 591.
[3] *Accidents Resulting in Injuries to Army Motor Cyclists*, 1949, London: H.M.S.O.

FERTILIZATION IN VITRO

Many attempts have been made to obtain *in vitro* fertilization of a mammalian ovum, and Moricard and Bossu[1 2] are the first to record their observation of the penetration of spermatozoa through the zona pellucida of the rabbit oocyte, and the penetration of a single spermatozoon into the oocyte-cytoplasm. Previous attempts to demonstrate fertilization *in vitro* have probably failed because the work was done in aerobic conditions, and it was not until Moricard and Bossu used a medium with an *r*H approaching 14, that is to say in relatively anaerobic conditions, that they were successful. They also improved on the technique of obtaining eggs by lavage from the Fallópian tubes. Instead they removed a small fragment of tube containing recent ova formed as a result of sterile coitus or injection of gonadotrophins. After suture of the ovarian end, a small quantity of liquid containing spermatozoa, removed from the vagina of another rabbit after recent coitus, is introduced through the uterine end of the tube, and this end is then sutured. The small sac is incubated under petroleum jelly at 37° C. for 5–7 hours. It is then fixed *in toto* and serial sections are cut and stained. The head of the spermatozoon is easily seen. It measures 7 μ by 3 μ. The zona pellucida appears as a clear ring, 10 μ deep. The authors have succeeded in observing passage of a spermatozoon through the zona pellucida in 15 out of 21 cases, and penetration of at least one spermatozoon into the ovarian cytoplasm in 5 out of 21 cases. Ovum segmentation was not observed to occur during the time these cultures were incubating—that is, a maximum of 7½ hours. Further experiments are planned on the physicochemical properties of the tubal secretion and also on the conditions necessary before segmentation of the fertilized ovum can take place.

Professor J. Henry Dible, F.R.C.P., will deliver the Humphry Davy Rolleston Lectures before the Royal College of Physicians of London, Pall Mall East, S.W., on Tuesday and Thursday, June 20 and 22, at 5 p.m. His subject is "Degeneration, Necrosis, and Fibrosis in the Liver."

[1] *Bull. Ass. Gynéc. Obstét. Langue franç.*, 1949, **5**, 484.
[2] Moricard, R., *Nature, Lond.*, 1950, **165**, 763.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

OSTEOARTHRITIS

BY

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Of the many forms of joint disease popularly described as "arthritis" the commonest is osteoarthritis, also termed in other countries hypertrophic or degenerative arthritis, both terms illustrating different aspects of the disease which might well be described in popular language as "wear and tear" arthritis. It is a disease for which treatment is rarely sought until well on in middle life, when symptoms may have been present for three or four years. It slowly progresses with age and varies in degree according to circumstances. This is a normal and irreversible process, and in that sense osteoarthritis is incurable, but many factors that affect the rate of degeneration can be influenced and the process slowed down, and it is of great importance that these should be dealt with at the earliest possible stage.

Congenital and acquired anatomical defects are important—for example, a shallow acetabulum, coxa vara and congenital dislocation of the hip, disorders of ossification such as Legg–Perthes's disease, and rarer defects. Rickets, by giving rise to curvatures of the long bones, genu valgum or varum, fractures of thigh or leg in early life, and severe degrees of flat-foot all tend to alter the skeletal architecture and the balance of hip and spine, thus throwing abnormal strain on the joint structures and accelerating the wear and consequent degeneration of cartilage and bone.

Trauma is one of the most important causes of osteoarthritis, though the graver accidents, fractures, etc., are less often the cause than the minor ones associated with occupation. The effect of heavy manual labour carried on in cramped postures, as is often the case in mining, is an important example, but there are many occupations not entailing any obvious physical effort but which by constant repetition of some apparently trivial movement may have an equally damaging effect. Careful inquiry into occupation, the form of activity, and the limbs and joints brought into play may throw much light on the cause of the disease and also be a guide to treatment by indicating alternative movements, spells of rest, or even complete change of occupation.

Heberden's nodes are a special form of osteoarthritis affecting the terminal joints of the fingers. They are much more common in women, to whom they often cause anxiety, and are regarded as being caused by rheumatoid disease, which is not the case. Commonly they first appear in middle life, often at the menopause, and there is a well-marked hereditary tendency. It is useful to remember that rheumatoid arthritis practically never begins in the terminal joints of the fingers but in the proximal phalangeal or metacarpal joints, spreading to the terminal joints at a later stage.

Osteoarthritis of the hip is one of the most serious forms of disablement. It was formerly called "malum coxae senile," or coxalgia, but is far from being a senile change and is often the result of congenital defects or of trauma which may be of a comparatively trivial nature. It is usually unilateral, but the alteration in balance and the effect of throwing the weight on the sound side to lessen pain sooner or later tend to set up symptoms on the other side, though this may be due only to periarticular fibrositis and contraction of the capsule. For the same reasons the knees and also the lumbar spine soon begin to show similar changes; the knees are also often affected by excessive kneeling.

Osteoarthritis of the spine is common, especially in the cervical and lumbar regions. It may be the result of accident, such as a fall on the back; develop gradually as a result of back strain, resulting from such causes congenital or acquired, as have already been mentioned; or be due to congenital defects or abnormality in the lumbo-sacral region. Shrinkage of the intervertebral disks as a result of nuclear prolapse or the ordinary changes of advancing years allows excessive play between the vertebral bodies, and the intermittent tension on the ligaments tends to the formation of osteophytes. It is important to note that even large hooked osteophytes may be symptomless and be discovered only by accident—a point of importance in compensation cases. In the cervical region the vertebral bodies may be much distorted owing to the great mobility and constant movement in all directions. Osteophytes form and may press upon or irritate the nerve roots as they emerge from the foramina, giving rise to referred pains and paraesthesias in the shoulders and arms and even to occipital headache. It is important to bear this in mind in cases with arm and shoulder pain.

Radiographs are essential for the diagnosis of osteoarthritis of the spine, and they should be interpreted by a radiologist or much may be overlooked. Views from the oblique as well as from the antero-posterior and lateral aspects are necessary for the examination of the foramina. Thinning of the disks is a feature of importance, since it does not occur in ankylosing spondylitis, an important point in diagnosis.

Symptoms and Clinical Signs

The disease is often advanced before advice is sought, as pain and stiffness only develop gradually. The first sign may be referred pain with no obvious relation to the affected joint; this is especially the case with nerve symptoms in the arms and shoulders. Pain in the knees may be the first indication of osteoarthritis of the hip, and if this is forgotten and the hip is not examined the loss of time in instituting proper treatment may be serious. Other common sites of referred pain are the adductor region of the thigh and the upper peroneal region. Pain in the groin, trochanteric region, and buttock is common. It is often absent at rest in the early stage but is brought on by walking; sitting down on a low seat may be easy but rising painful, the reverse being usually the case in sacro-iliac arthritis. Pain is felt if the weight is thrown on the affected side, but in sacro-iliac disease the pain is more often induced if the weight is on the unaffected side. An important early sign of arthritis of the hip is that termed by the French as *le signe de soulier*—that is, increasing

difficulty is met with in tying the shoe on the affected side, the knee is flexed and the foot is drawn back in order to reach the shoe, but even this soon becomes impossible.

Restriction of movement at the hip develops early from contraction of the capsule due to periarticular fibrositis, from the formation of osteophytes at the edge of the acetabulum, or from congenital defects which have slowly increased. It often happens that a full degree of flexion is present long after lateral and rotatory movements have become much restricted; limitation of extension develops imperceptibly and may not be noticed until it becomes marked.

Examination in the prone position is the best way to demonstrate deficiency in abduction, which is generally the first to appear, followed by internal rotation. The knee is flexed to a right-angle and the range of movement in various directions is compared with that of the sound side. The patient is then turned on to his back and extension tested, care being taken to maintain the normal lumbar curve; measurements should then be taken to detect any shortening. A moderate degree of wasting may be noted in the gluteal muscles and the adductors of the thigh. General constitutional symptoms are absent.

Limitation of movement in osteoarthritis of the spine is often slight or may be absent, but forced movement may be painful, as a degree of fibrositis is often present. Referred pains from pressure on the nerve roots may be present if there is much thinning of the disks; osteophytes even of large size may not cause any inconvenience. Paraesthesias and referred pains may be the first sign when the cervical vertebrae are affected, but the reflexes are rarely altered.

Differential Diagnosis

Ankylosing spondylitis presents the chief difficulty. It usually occurs at a much earlier age and is accompanied by constitutional symptoms in the active phases, but these often alternate with periods of quiescence wherein lies the possibility of confusion. The sedimentation rate is usually increased, slight pyrexia may be present, and pain is more severe and continuous even apart from movement. Radiographs will confirm the diagnosis. The intervertebral disks maintain their full width in the ankylosing form but are crushed or narrowed in osteoarthritis in which ankylosis does not take place except in the form of fusion of contiguous osteophytes.

In elderly patients the possibility of malignant growths must be borne in mind, and crush fractures of the type of Kümmell's disease may also present difficulty. Chronic osteomyelitis and typhoid spine as well as rarer disorders may be met with, but radiographs should never be omitted if there is any doubt.

Arthrokatadysis, a condition in which the floor of the acetabulum projects into the pelvis, is a not infrequent congenital defect; it is sometimes called protrusio acetabuli or Otto's pelvis. It leads gradually to deepening of the joint cavity, with thinning of the articular cartilage and lipping of the rim of the acetabulum causing a steadily increasing limitation in the range of movement at a much earlier age than in osteoarthritis of the usual type.

Treatment

The first essential is to realize that though cure is not possible some relief and slowing down of the progress of the disease may generally be achieved, and that the earlier treatment is begun the better the result will be. The history should be carefully investigated, especially with regard to occupational effects and minor accidents which may have been so slight as to be forgotten. Careful examination of the movement of the joints in all middle-aged patients complaining of rheumatism of any kind will always prove worth while, and radiographs are desirable in cases of stiffness of the back, neck, or hips; in other joints clinical examination may suffice.

Rest for the affected joints is important, but invalidism must be avoided; change of occupation may be sufficient. Standing for a long time is harmful, and walking must be limited in arthritis of the lower limbs, especially with weight-carrying. The footwear should receive attention in these cases. Orthopaedic treatment of fallen arches, hallux valgus, etc., will lessen strain on the knees, hips, and back. Where there is shortening of one leg from any cause thickening of the heel of the shoe and possibly of the sole as well will give much relief, and a rubber heel or a pad of spongy rubber inside the shoe will lessen jarring.

Exercises are important, especially of the hip, in order to prevent contraction of the capsule, and should be carried out night and morning with the patient lying on a firm mattress or the floor. Abduction, adduction, rotation, and full extension are the most important, but too many or too strenuous exercises may have the opposite effect to that desired. The exercises should be taught by the doctor or a qualified masseur. Some degree of loss of extension of the knees is not uncommon and must be guarded against or treated by means of plaster-of-Paris splints worn at night or by a support of the Howard Marsh cage type hinged at the joint with a clip to fix the hinge when walking. This will prevent lateral play and give a sense of security, especially in those cases in which the knee is apt to give way. A walking calliper to take the weight of the body off the hip and knee will give relief from pain in coxalgia, though patients often object to wearing them. Surgical corsets are not generally advisable in osteoarthritis of the spine, but for the cervical region a leather collar may be desirable, and a light sling made of a band of webbing with a loop at each end may be helpful by taking the weight of the shoulder and arm; it need not be worn continuously.

Massage should be directed to relieving muscle spasm or wasting rather than to the joints; mild surging faradism and remedial exercises may usefully be combined with it. Occasional courses of ten to twelve treatments are better than months of attendance at a physiotherapy clinic in most cases, as this tends to create an invalid outlook, whereas the object should be to encourage an active life so far as is possible.

Hydrotherapy and spa treatment, especially the deep-pool bath and douche massage, are of great value. The deep pool, by reason of the support given by the water, makes exercises much easier and thus increases the range of movement. After the preliminary treatment at a spa or clinic where such treatment can be obtained a visit to a swimming-bath once or twice a week may be advisable, but long immersion must be avoided. Turkish baths, especially in individuals who are overweight or who take too little exercise, may be used with advantage if there is no cardiac disability. Simple hot baths at home are used so often for relief of pain and stiffness as to need no further mention: the addition of washing soda or Epsom-salt often seems to enhance their effect.

Electrotherapy

For superficial joints, especially the knees, cataphoresis with salicylate of soda often gives relief from pain, while iodide of potash tends to promote absorption of exudation and fibrositic thickening around the joint. The proprietary preparation "T.C.P.," which supplies iodine, chlorine, and

salicyl ions, is useful, as it combines both these effects. A qualified physiotherapist can sometimes be found to give this treatment at home if a physiotherapy clinic is not available. Short-wave diathermy is widely used for the relief of pain, especially in the hip and back, and is more useful in these joints because of its deep effect. *X*-ray therapy is sometimes used for the relief of pain in the hip or back, but is less effective than in ankylosing spondylitis.

Injection Treatment

A method which has recently come into vogue is injection into the joint cavity. It was first used with sodium acid phosphate and later with lactic acid, but procaine has been found to give equal relief from pain, though possibly not the other results which are claimed to occur—namely, the formation of a layer of dense fibrous tissue in place of the destroyed cartilage, arresting in some degree the degenerative process. The treatment must be followed by passive movements, manipulation, and exercises. Much skill is required to ensure that the needle enters the joint, which may be more difficult because of the thickening of the capsule, and if this is not achieved the result may fall short of expectations. The injections should be repeated at intervals, but unless relief is experienced they should not be continued.

Another method which is sometimes effective and calls for less expert skill is the injection of iodine in oil in the vicinity of the joint. It was first practised in France, lipiodol being the preparation used; English equivalents such as "iodatol" are now available. I have used this method in suitable cases, especially those in which periarticular thickening gives rise to pain and stiffness before there is much bony change, and good effects have been obtained; some cases have been under observation for as long as fifteen years and have retained a fair degree of mobility. The injection gives relief from pain and stiffness for three or four weeks, when it may be repeated, the intervals being gradually increased. The procedure is simple: the oil, which is viscous, is warmed and 2 or 3 ml. is injected deeply into the buttock in the region of the joint, with the usual precautions. Absorption is slow, and it is probable that the administration of iodine in this way is the best means of securing its systemic action, which is believed, especially by French authorities, to be of value.

Other Measures

Drugs by the oral route are of little value except for the temporary relief of pain and stiffness, aspirin alone or with phenacetin or codeine may be taken, but opiates should be avoided as they are apt to cause constipation and are habit-forming. Iodine in the form of the tincture, the iodide of potash, or one of the proprietary preparations may be useful, but it is difficult to assess its value.

Diet does not call for consideration except in patients who are overweight, and since weight-bearing is an important contributory factor this should receive attention. Salt may be reduced with advantage in such cases to lessen water retention.

Surgery may be called for when pain is severe or deformity serious, and if it is to be considered the earlier it is undertaken the better the results are likely to be. It is a matter for an orthopaedic surgeon to determine the form it should take, but the results are often disappointing; to remain in hospital in splints for a long period is a serious matter. The principal procedures now in vogue are neurectomy of the obturator nerve and the articular branches of the anterior crural and sciatic nerves; arthroplasty, inserting a metal cap (vitalium) between the head of the femur and the acetabulum; and excision of the head of the femur in order to form a false joint.

Early treatment, rest for the affected joints by attention to occupation, splints, and supports, appropriate exercise to cope with the threatening limitation of movement, combined with a courageous and persevering attitude on the part of the patient, will give worth-while results.

MEN AT WORK*

BY

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(From the Social Medicine Research Unit, Medical Research Council)

These remarks deal with some problems of men at work in general, and with those of one man at work in particular—the industrial medical officer.

Our Present Situation

To-day we have full employment. A greater number of people are employed, output for every man employed is higher in almost every industry, and our total production is greater than ever before in peacetime. And yet output still falls short of our needs. In fact, our balance is so precarious that unless we do produce more, and more cheaply, we may find ourselves short of raw materials, and facing unemployment, lower standards of living, and a threat to the whole structure of the welfare State.

The question is: "How are we to produce more?" It may be answered in many different ways. Economics, long ago called the "dismal science," has various solutions to offer, including a "healthy dose" of unemployment. More realistically, economists favour the wider adoption of payment by results, at present restricted to a minority of wage-earners. This would undoubtedly be a useful measure in the struggle against inflation and might in many industries help to raise output, but it could hardly be an adequate answer to our problem. During the war we progressed far towards achieving a true harmony between individual purpose and social purpose. To-day there appears to be a serious discrepancy between what the community needs and what its individuals in their various groups are able or prepared to contribute. And it is doubtful whether such a social malaise can be cured in terms of wage-packets or fear of the "sack." This problem of "incentives" demands some hard thinking, in terms of man and work, industry and community.

The Standard of Living.—The basic objective of work is to provide the worker and his family with necessities and amenities as dictated by individual and class standards. We have lived for long in an expanding economy in which yesterday's luxuries became to-day's necessities. Many of these necessities (including expensive "indulgences," holidays, and some saving) are not now being at all easily provided; the population to-day at most levels of income, on the standards it at present wants, is in fact "broke." This makes our predicament all the more incongruous: the community requires more than its individuals are prepared to contribute; its individuals require more than the community can at present provide. The issue is clearly not

*From an address to the Association of Industrial Medical Officers, January 27, 1950.

one of economics alone. It may be that the need for leisure is becoming dominant, since work in many cases is felt to be so frustrating.

Some Facts and Theories

Can medicine, and in particular industrial medicine, help? Medicine is concerned with human beings, and if production is related to their health and happiness it is medicine's affair. The more we learn of people the clearer it becomes that work is in fact very much related to health and happiness—our work affects our health, and how healthy we are affects our work. We may therefore, by drawing on our own ideas and on the experience of the other social sciences, begin to formulate a working philosophy for those of us who practise industrial medicine. Here, in brief, are a few chapter headings.

"Work is the Inevitable Condition of Human Life."—This is surely obvious enough; and now psychiatry is increasingly emphasizing the significance of work for human motivation and in expressing fundamental drives, considering it next in importance only to the family. But while the family, in our time, represents the main source of happiness, work only too often seems to be a major frustration.

The Physiological Requirements.—By now industrial medicine and its allies have acquired a great deal of knowledge of the physical environment in relation to health at work, though much of what we know is not being applied. It still comes as a shock to find, on visiting factories, how even the elementary physiological requirements are so often ignored. Too many of our factories, and not only the smallest, are too slummy. Even less are many advances of machine design and those from the psychology laboratories being applied. Are we, who are so interested in efficiency and economy of effort, doing all we can to educate management? Conditions at work are our first responsibility, and this means much more than the prevention of recognized hazards and the watch for new ones.

Welfare.—Similarly, in welfare and the provision of amenities we have much leeway to make up. Fortunately, the shortage of man-power is stimulating many managements who otherwise would not have had the good sense to act. Industrial medicine is already deeply committed here. How distinct, in fact, the medical, welfare, and personnel departments should be is one of the great questions for to-morrow. We must, however, already go forward from these well-defined physical and psychological requirements and from the limitations of the "welfare" outlook. As has been shown so clearly in the undermanned industries, improvement of conditions of work and pay is not enough.

Work Satisfaction.—Vocational guidance, job analysis, and placement examinations are helping us to provide people with jobs that suit them. But work involves very much more than is yet comprised by these techniques. Studies are now required, on the one hand, of the emotional and social "needs" that men bring to their work to-day, and on the other of what might be called the relevant "properties" of different jobs. So far we have only rather sketchy ideas of what these "needs" are, but we regard them as deriving from basic human instinctual drives, modified in the long history of our society. What are they to-day? Security, approval, status, authority, responsibility, achievement, the "instinct of workmanship"? And service? What happens to such needs in mass-production industry? Can they be satisfied in the blackcoated jobs or in the lower managerial posts? How do the professions compare with the trades and with unskilled labour? What balance of satisfaction and frustration are men achieving in the work itself, and in its social relations? Have we reached a situation where for many the main satisfactions of the job must come from the human contacts and relationships incidental to the work? And, if so, can we any longer afford to consider them incidental?

Living in Groups.—By now we all recognize that the social life is as "natural" as the private; that "belonging" to a group is a rich source of emotional security. None of the statistical indices of industrial health are at all perfect, but we know that in civil as much as in military life there are happy and unhappy groups, well and sick, integrated and anarchic, effective and ineffective, productive and less productive; and that individual health depends much on the groups of which one is a member. Unfortunately, we know less of the factors making for good morale and the development of healthy well-knit groups than of the conditions leading to hostility, frustration, and anarchism. We have, for instance, little more than intuition to guide us in dealing with problems of leadership and its functions at the different levels of industry.

Democracy in Industry.—To-day we have political but little industrial democracy. It is conceivable that there can be healthy and effective small groups in a factory, whose members take no further part in its affairs. But it is unlikely that with such an artificial brake on spontaneity there can be any real identification with the purposes of the factory as a whole. And it is unlikely that to-day's divergence of purpose between the community and its individuals can be bridged unless people feel personally involved in what happens at the levels between the group of mates on the shop floor and the big society of the industry and community as a whole, so often misunderstood as the hostile and impersonal "they." Unfortunately, no generally effective means have yet been devised to meet this exceedingly difficult problem, either in private or in nationalized industry. Is this our business? Surely it is. With the fragmentation of so much of our social life, "joint consultation" and similar movements have become as crucial to health as they are to production. They could help men to make use of their abilities; to grow to maturity, adulthood, and responsibility; to co-operate in service; and to develop stronger bonds between the individual and his society by breaking down isolation and promoting community spirit.

Summing Up.—Our experience—or is it our faith?—suggests that mature human beings, physically healthy, secure in well-integrated groups and living fully in a democratic society which appreciates the worth of work, will be productive in as "natural" a way as men appear to be in primitive societies; will contribute what the community needs and expect only what society can provide; and will forget past grievances. The hope is that, with everyone taking part in the choice of means as well as ends, we may one day combine the advantages of both modern and primitive communities. So far, no expanding and mobile society such as ours has ever achieved such conditions, nor will they be brought about by the welfare State of itself, though its very survival depends on our discovering a new ethic of work and dynamic of efficiency. We must therefore be prepared for as great changes in the social structure of industry, to promote *social* health, as have already been necessary in its physical aspects, so that physical health can thrive and work can be done efficiently. So far the changes have been largely confined to administrative control.

The I.M.O. and the Production Drive

These remarks are largely theory; such facts as we possess have mostly been demonstrated in other countries and are not necessarily true of ours. We cannot yet formulate a coherent and immediate policy which will contribute to production; in emphasizing immensely complicated human relationships we cannot provide such concrete answers as unemployment or bonuses—the whip or the carrot. In fact, we are answering the question, "How can industrial medicine help in production?" by asking another, "What can we do to promote mental and social—as well as physical—health in industry?" We must always remember that as doctors our first charge is the well-being of the men at work. But we must not forget the cost at which the greatest increase in production was achieved in the nineteenth century and the legacy with which we are left, nor indeed that the modern movement in industrial medicine derives from the disregard of such things in the first world war.

Three Errors of Industrial Medicine

The I.M.O.'s method is the doctor's method—to investigate and treat, to teach and guide. With this method in mind, review of our problems suggests that there are at least three common errors in industrial medicine—errors to-day, but, I fancy, to-morrow's heresies.

1. Prevention—or Prevention and Treatment.—We are agreed that the function of industrial medicine is to prevent illness and accident and to promote health as best we know how; but, because treatment is thought of only in individual terms and we must not duplicate the work of the G.P. or the hospital, the error is common of soft-pedalling the therapeutic function of the I.M.O. and restricting it so far as possible to first aid and rehabilitation. Treatment, however, will become as much interpersonal and social as individual, and the I.M.O. of to-morrow will have to practise therapy as conscientiously as to-day he avoids it. But it will be *social* therapy, not physical and individual, and will deal with difficulties of human relationships, with emotional problems (for these always have social implications), with stress in groups and between groups and individuals, inadequate leadership, poor morale, and so on. The I.M.O. indeed often already fulfils this function most usefully without being aware of it. To-morrow, if he doesn't do it, other workers will be brought in for this purpose—who will be without our advantages and may have less than our wisdom.

2. "Function of Management"—or Social Service.—The purpose of words is surely to convey meaning and to help us in our thinking. Industrial medicine is so much more than a function of management that it is strange that so many of us stick to so inaccurate a definition. The industrial health service is usually paid for by industry (that is, workers, capital, management) to promote the well-being of those in industry and, to a smaller degree, of their families. In fact, it is a public, a community, a *social* service which is being pioneered in one of our typically British ways. It is time we so regarded and declared ourselves. If we continue to align ourselves with management our future as social therapists will be difficult indeed, as part of our strength lies in our neutrality.

3. Specialist—or Wholist.—Industrial medicine is a specialty, it is commonly said. This is an error not only because it confuses the specialist with the expert, which doesn't matter, but because it misses the important point that industrial medicine belongs to an era in medicine that has come *after* the rise of specialism. We need specialists of all kinds, but we now recognize that specialization is not enough; that is why medicine is now beginning to develop along new lines. We have found that we also need a new type of doctor who can see things in the round, who tries to understand the human being as a person in his environment, who is interested in the psychological as well as the physical, in groups as well as in individuals—because all these make us what we are. Of course, it is desirable that all doctors, even specialists, should practise something of such comprehensive, social medicine, and in time we hope that all will; but for the I.M.O. it is already an inescapable duty. The I.M.O., like the modern paediatrician, for example, should be defined not by any specialism or technique, but in terms of his versatility, the breadth of his interests, the depth of his understanding. This is going to be a hard job, because we have none of us been educated that way.

Industrial medicine arose in response to a social need. If it can develop and respond to the new and rapidly changing needs of our time its future as a constructive element in the community is assured.

ASSOCIATION OF SEA AND AIR PORT HEALTH AUTHORITIES

51st ANNUAL MEETING

The Association of Sea and Air Port Health Authorities of the British Isles held its fifty-first annual meeting at Grimsby on June 7, 8, and 9 under the presidency of Councillor A. E. KELHAM, chairman of the Grimsby Port Health Committee. Alderman T. F. Regan, of Manchester Airport, was elected president for the year 1950–1, Dr. H. C. Maurice Williams, O.B.E., was re-elected honorary secretary, and Dr. W. M. Frazer, O.B.E., was re-elected honorary treasurer.

Councillor KELHAM, in his presidential address, reviewed the activities of the association during the past year. He referred to the efforts that had been made to unify the procedure on food inspection of crew's provisions. He mentioned the representations that had been made to the Ministry of Health in connexion with vaccination against smallpox for passengers arriving in this country from epidemic areas. Another important matter dealt with was the recommendation submitted to the Minister of Food about the control of inedible fats. Consideration was also given to the draft regulations in connexion with the Sea Fish Industries Bill, the Milk (Special Designations) Regulations, the Metallic Contamination of Food, the Whalemeat Regulations, the Hygiene of Ships, and the tracing of Tuberculosis Contacts.

Dr. L. THOMAS, senior medical officer, London Airport, followed with a paper entitled "The Medical Procedure at Northolt Aerodrome, with Special Reference to the Aircraft Regulations, 1950." Dr. Thomas emphasized the difficulties of health control because of the speed of travel. Passengers generally arrived in this country from areas where major infections such as smallpox, typhus, cholera, yellow fever, and plague are rife. A total of 46,097 passengers, or over 12% arriving in this country from overseas, come from or through areas where these major infectious diseases are endemic. The health control procedure was closely integrated with the examination of passengers by the immigration and customs authorities. He described the revised procedure under the Western Union Agreement whereby medical inspection is limited to the first port of entry within the Union.

Mr. J. D. SYME, chief port health inspector, Grimsby, spoke on the unsatisfactory nature of existing legislation on crew accommodation on merchant vessels. He was followed by Mr. H. W. WILSON, who gave a comprehensive account of the fishing activities in the port of Grimsby, where over a quarter of a million tons of fish are dealt with annually.

Dr. ANDREW SEMPLE, deputy medical officer of health, Liverpool, drew attention to the difficulties of the ship's surgeon in

the event of an outbreak of suspected infectious disease on board, and advocated the production of a suitable manual to deal with this problem. International certificates of immunization were discussed, and a scheme recently introduced in certain of the larger ports for the purpose of tracing tuberculous contacts was described. He made a strong plea for the routine use of mass miniature radiography for merchant seamen.

Dr. G. BUCHANAN, medical officer, National Dock Labour Board, in a paper on "Medical Services in Docks," observed that the care and welfare of the dockers had not progressed at the same rate as that in other industries. He quoted statistics showing the mortality rates in various groups of dock workers between the ages of 20 and 65. These rates were higher than the general rate for all males within the same age range—for example, dock workers gave a rate of 137 and stevedores a rate of 220 compared with the rate for all males taken as 100.

Dr. Buchanan described in detail the medical services set up by the National Dock Labour Board, which was instituted in June, 1947. One of its duties is to promote the general health of the dock worker, to provide for the emergency care and treatment of injuries and sudden sickness at work, and to assist in the rehabilitation of the sick and injured worker. The National Board had appointed full-time officers at Tyne, Tees, London, South Wales, Liverpool, and Scotland, and had set up medical centres in all the principal ports of the country where full- or part-time officers were employed. In 1949 the medical centres dealt with 175,902 treatments. There had been an appreciable reduction in the accident rates throughout the ports, particularly in connexion with septic conditions.

PUBLIC HEALTH ENGINEERING

POSTGRADUATE COURSE IN LONDON

Funds provided by the Rockefeller Foundation have enabled the Imperial College of Science and Technology, with the co-operation of the London School of Hygiene and Tropical Medicine, to develop a new branch of postgraduate education —public health engineering. Experience in the U.S.A. has shown that the teaching of this subject is best organized as a joint venture between the university schools of engineering and of public health. Not only does such an arrangement help towards the solution of problems common to both professions, but it increases the interest of the public generally in matters relating to health.

The first full-time postgraduate course in public health engineering will start in London in October. It will be centred at the civil engineering department of the City and Guilds College, and will be under the general supervision of the professor of civil engineering. A public health engineering advisory committee has been established by the governing body of the Imperial College of Science to assist in matters of policy and organization. It includes representatives of professional and scientific bodies and independent members concerned with public health engineering.

The course is primarily intended for students holding a first degree in civil engineering or an equivalent qualification, and satisfactory completion of the course will qualify for the award of the Diploma of the Imperial College (D.I.C.). The course will include teaching in the following subjects: principles of public health engineering; public health and local government; statistics; statistical epidemiology; bacteriology; introductory entomology; examination of water and sewage; water supply and sewage treatment; occupational health; and tropical hygiene. From the above list of subjects it can be seen that public health engineering is not confined to domestic water supplies and sewage disposal; its aim is to improve environmental sanitation, which was defined by a W.H.O. Expert Committee as "the control of all those factors in man's physical environment which exercise or may exercise a deleterious effect on his physical development, health, and survival." For this reason the range of subjects covered in the public health engineering course has to be very wide, since the engineer has a responsibility, direct or indirect, in many matters affecting the health of the community.

AUSTRALASIAN MEDICAL CONGRESS

(BRITISH MEDICAL ASSOCIATION)

SEVENTH SESSION

The Seventh Session of the Australasian Medical Congress (British Medical Association) was held at Brisbane, Queensland, from May 27 to June 3 under the presidency of Dr. ALEXANDER PATERSON MURPHY, who was until recently professor of medicine in the University of Queensland.

This was the first occasion on which the Congress, under the aegis of the British Medical Association, has been held at Brisbane. Under the old regime the last Congress of the series was held at Brisbane in 1920. On that occasion it was resolved that all future congresses should have a British Medical Association character. The title of the Congress was changed to "Australasian Medical Congress (British Medical Association)" and the organization was placed under the control of the Federal Council of the British Medical Association in Australia.

The session was a great success. More than 800 members enrolled, some coming from Western Australia, more than 2,500 miles away, and some from New Zealand. The Council of the parent body was officially represented by Dr. E. A. Gregg, its chairman; Dr. Angus Macrae, Deputy Secretary of the B.M.A., was also present. The second meeting of the British Commonwealth Medical Conference was held at Brisbane just before the Congress, and all overseas delegates to that gathering were made honorary members.

The inaugural meeting was held at the City Hall, Brisbane, on the evening of Monday, May 29, when the session was officially opened by His Excellency Sir John Laverack, Governor of Queensland, in the presence of the Premier of Queensland, the Right Honourable E. M. Hanlon, and the Lord Mayor of Brisbane, Alderman J. B. Chandler. Sir JOHN LAVERACK welcomed the visitors to Queensland and referred to the debt which humanity owed to the medical profession and to the part which doctors had taken in the two world wars. He hoped that the Congress would be a success and that nothing would happen to interfere with the holding of the Eighth Session, which, he understood, was to take place in 1952.

President's Address

Dr. ALEX. MURPHY delivered the President's address. He first asked the Governor to convey to His Majesty the King, who was Patron of the British Medical Association, expressions of loyalty and affection from the gathering. After reference to the amazing advances in medicine during the first half of the twentieth century, Dr. Murphy reminded his audience that Nature exacted her toll from man's ingenuity and that cardiovascular disease had shown a staggering increase in the previous 25 years. Medical men enjoyed the doubtful privilege of providing the highest occupational mortality from coronary arterial conditions, and it was not without interest to try to uncover the causes of the increase.

Dr. Murphy thought that man's discovery of how to generate and harness electricity provided the explanation. Modern inventions had had their cumulative effect on the former tranquillity of life. In all modern change the doctor had fared ill. He was at the continuous mercy of the telephone, especially the automatic variety, whose summons could not be disregarded. His conveyance was a motor-car, which almost invariably he had to drive himself; disaster lurked at every corner, so that if he had his mind on the troubles of his patient he was apt to find himself in the queue at Charon's ferry. Speed permitted contact with far more patients than formerly and periods for reflection between tasks had been abolished. The doctor was harassed in many other ways, and it was almost easier for the camel to perform the proverbial feat of passing through the needle's eye than for a medical practitioner to find a bed in a private hospital for a patient in an emergency. To overwork were added frustration and its sequel, exasperation.

Medical literature had attained colossal proportions. Progress was so rapid that in many respects textbooks were out of date before they left the press, and the doctor struggling to keep abreast of medical knowledge had to choose either to

be drowned by the weight of his conscience in an ocean of journals, or, in order to survive, to abandon the attempt and so to drift into a Sargasso Sea of mental stagnation. Medical men had no monopoly of these conditions and their lead in mortality statistics was but a short one. Other factors mentioned by Dr. Murphy were the immoderate use of tobacco, and noise. The former put great stress on the vessels of those whose vascular inheritance was not flawless; recent animal experiments in regard to the latter had shown that noise alone could derange the mind and even lead to death. The outcome of all this was tension, restlessness, and irritability. The best defence would appear to be the inheritance of a faultless cardiovascular system, but man could not choose his parents. Shakespeare, that master of prophecy, must have envisaged the present era when he wrote: "Farewell the tranquil mind; farewell content."

The answer to any inquiry for a remedy was, Dr. Murphy believed, provided by the word "leisure." At the present time the brain worker was starved of leisure, that time for unhurried thought, which was his lifeblood. The *Shorter Oxford English Dictionary* defined leisure as "freedom or opportunity to do something"; this definition was preceded by a symbol indicating that it was obsolete and at once invited substitution of "freedom or opportunity to watch someone else do something" as a modern version. Leisure in its true sense was not synonymous with indolence. The manner of its expenditure should be congenial, but on the whole it should be productive or it might prove worse than useless. The outcome should be a sense of gratification or enhanced self-respect, arising from the belief that some contribution, however small, had been made to knowledge, or to the happiness or welfare not only of the individual but of his fellows. He was convinced that without a high degree of self-respect and mutual esteem no community could hope to survive, and that the amount of leisure it took and the manner in which leisure was expended might determine its fate. Those few were to be greatly envied who, though reared in "hours of change, alarm, surprise," had been able to possess themselves of celestial serenity of spirit. Of these alone or almost alone might it be said in the words of Coleridge:

> "For they on honey-dew have fed
> And drunk the milk of Paradise."

THE SCIENTIFIC SECTIONS

The following were the sections of Congress: Anaesthesia; Dermatology; Medical Literature and History; Medicine; Naval, Military, and Air Force Medicine; Neurology and Psychiatry; Obstetrics and Gynaecology; Ophthalmology; Orthopaedics and Physical Medicine; Oto-rhino-laryngology; Paediatrics; Pathology, Bacteriology, Biochemistry, and Experimental Medicine; Public Health, Tuberculosis, Tropical Medicine, and Industrial Medicine; Radiology and Radiotherapy; Surgery.

All sections met in a plenary session which took the form of a panel discussion on rheumatism. The chairman of the panel was Dr. S. A. Smith (Sydney) and the members were Professor Lorimer Dods (Sydney), Dr. Selwyn G. Nelson (Sydney), Dr. J. H. Young (Perth), and Dr. R. F. A. Strang (Melbourne). This was the first occasion on which a presentation of this kind had been adopted for a large medical gathering in Australia, and it was generally agreed to have been successful. Among the subjects on which the members of the panel were asked to express their views were the finding of a satisfactory name for what was known as acute rheumatism or rheumatic fever, the diagnosis of acute rheumatism in the absence of limb and joint pains, the social incidence of the disease in Australia, the age incidence, the mode of action of salicylates, the dosage of salicylates, the use of salicylates other than the sodium salt, the use of antibiotics, the diagnosis of carditis, the criteria of quiescence, the prognosis for a child after its first attack of rheumatism, possible measures to diminish the risk of recurrence, the light thrown on the nature of rheumatoid arthritis by recent work on cortisone and A.C.T.H. and the removal of septic foci, osteoarthritis and its treatment, the recognition and treatment of ankylosing spondylitis, the diagnosis of acute gout, and the management of chronic gout.

One of the important features of the Congress was the reintroduction of a Section of Medical Literature and History. The president of the Section was Dr. W. E. L. H. CROWTHER, of Hobart, an authority on the early history of medicine in Tasmania. Among the papers presented to this section was one by Dr. ROBERT SCOT SKIRVING, of Sydney, who gave a description of medicine in New South Wales in the years 1880–1900, and another by Dr. D. GUTHRIE, of Edinburgh, on "History as a Basis of Medical Education." Dr. Guthrie held that the greatest need of medical education was some common ground on which the various sciences might meet and that history alone could provide such a meeting-place. The gulf between medicine and the humanities was far too wide and was becoming still wider; history, if properly taught, could help to bridge the gap. He made a plea for the writing of a history of the medical schools and hospitals of Australia and New Zealand.

In his president's address to the Section of Pathology, Bacteriology, Biochemistry, and Experimental Medicine, Dr. REGINALD WEBSTER, of Melbourne, discussed perspective in pathology. He made a plea for the recognition of the clinical pathologist as a consultant of standing equal to that of consultants in other spheres of medical practice. In regard to the training of consultants in clinical pathology, Dr. Webster advocated the curriculum drawn up in England by the Association of Clinical Pathologists in 1947, but thought that a further year should be added for Australians to gain experience by travel in other countries.

Dr. BRUCE ROBINSON, of the Pathology Department of the University of Melbourne, dealt with the diagnosis and management of sarcoidosis in the light of 30 cases in which the diagnosis had been proved. Dr. E. H. DERRICK and Mr. H. E. BROWN presented a paper in which they surveyed human brucellosis in Queensland. They reported the occurrence of 25 cases over a period of 14 years.

Dr. H. F. MAUDSLEY, in his president's address to the Section of Neurology, discussed the evaluation of neuropsychiatric symptoms. Dr. Maudsley's father, Sir Henry Maudsley, had been president of the same section in the Australasian Medical Congress held at Brisbane in 1920.

Among the subjects discussed at combined meetings of sections were peripheral vascular disease, peptic ulcer, coal-miner's pneumoconiosis, carcinoma of the breast, thoracic surgery in children, bearded women, infection in midwifery nursing, carcinoma of the larynx, and headache. Dr. R. J. WALSH, of Sydney, in a paper on homologous serum hepatitis, reported its occurrence in approximately 2.5% of patients who received pooled human serum by transfusion; the condition was rare after blood transfusion.

The Congress Dinner

The Congress Dinner was held on June 1, 450 members being present. Dr. Alex. Murphy, the president, occupied the chair. The toast of the British Medical Association was proposed by the Right Honourable E. M. Hanlon, Premier of Queensland, and Sir Victor Hurley, president of the Federal Council of the British Medical Association in Australia, replied. In reply to the toast of the visitors, Dr. E. A. Gregg referred to the relations between the parent body and the Australian Branches and to ". . . ties which, though light as air, are as strong as links of iron." He spoke of the heritage which medical men and women of the present day had received from their predecessors in medicine, and concluded by quoting the motto of the city of Belfast, his own city, which asked: "What shall we give for all that we have received?" Dr. T. C. Routley also replied for the guests and spoke of the efforts of the World Medical Association to promote intercourse and understanding between the members of the medical profession in all the participating countries. His remarks and those of Dr. Gregg were received with great enthusiasm.

The autumn weather of Queensland is a delight to Australians from other States, and overseas visitors enjoyed a good sample

of it. The hospitality of Queensland people is open-hearted and generous, and the social fixtures of the Congress—the inaugural meeting, the public lecture, and the ball—were preceded by convivial gatherings.

The Eighth Session

The Eighth Session of the Australasian Medical Congress (British Medical Association) will be held at Melbourne in 1952, a year which will mark the centenary of the Medical Society of Victoria. This body coexists with the Victorian Branch of the Association.

KING EDWARD'S HOSPITAL FUND

SECOND YEAR OF NATIONAL HEALTH SERVICE

In taking the chair at the annual meeting of King Edward's Hospital Fund on June 6, H.R.H. the Duke of Gloucester said that the Fund stood just a little aside from the National Health Service and could claim some independence of judgment. The change-over from traditional patterns to an entirely new system of hospital care had been accomplished smoothly, and with improvements in some directions, notably in the staffing of hospitals. But there had been a steep increase in costs. The Fund had long been aware that a limit would have to be laid down, and when that point was reached it would have to be decided how the total sum could be handled with the desired flexibility. That was the situation to-day.

"We at the King's Fund see no really satisfactory solution that does not involve a break with the established methods of controlling public moneys. Will the regional boards be given definite round sums on an annual basis which they can pass on to the hospital management committees, and will the hospital management committees be given freedom to deal with these round sums as they think fit?"

The Duke went on to say that the Minister of Health had asked the Fund, together with the Nuffield Trust, to conduct a costing investigation in a number of hospitals, and this the Fund was glad to do because it believed that once the advantages of a departmental system of accounts were realized the whole scene would be transformed. It would then become possible to allocate money to hospitals rationally, and efficient administration would replace the hit-or-miss methods of to-day.

Speaking of other enterprises of the Fund, he mentioned the establishment of a staff college for hospital administrators, which he believed would become a focus of responsible opinion on hospital administration as well as a means of training the younger men. The Fund had been fortunate in enlisting as a part-time officer Sir Wilson Jameson on his retirement from the Ministry of Health. He would bring his great abilities to bear on certain educational efforts of the Fund which were still young and had to get firmly on their feet, and he would also succeed Sir Hugh Lett, whose retirement was much regretted, as chairman of the nurses' staff college.

A financial statement was presented by Sir Edward Peacock, the treasurer, and the annual report by Sir Ernest Pooley, chairman of the management committee, and, after a few remarks by Lord Webb-Johnson and others, these were adopted. A vote of thanks to the Duke was moved by the President of the Royal College of Physicians, Dr. Russell Brain, and seconded by the President of the Royal College of Surgeons, Sir Cecil Wakeley.

Subscriptions and donations to the Fund have never been large, since the Fund has refrained from active competition with the hospitals in the search for subscribers. They fell off with the inauguration of the National Health Service, but have risen slightly in the second year, and now stand at some £17,000, rather less than half the annual pre-war average. The main income of the Fund comes from investments—nearly a quarter of a million. In addition a sum of £150,000 was received during the year from the Nuffield Trust for the special areas (so far £1,250,000 has been received from that source), and the legacies of the year contributed over another quarter of a million.

Homes for Aged Sick and for Convalescents

Two large grants from the Fund were made in 1949—one of £250,000 for the provision in the London area of a limited number of homes for the aged sick, and the other of £100,000 for convalescent homes. The homes for the aged sick are intended for those who have reached the end of useful hospital treatment and require something between a hospital and a home—not a convalescent home, as they are expected to make a long stay, and not a home without nursing supervision, for some of the patients need watching and occasional nursing as well as ordinary care. The quarter of a million will provide 12 homes, each containing 25 to 30 beds. Their location has been a matter of some difficulty. Every hospital management committee could show evidence of the need for such a home, but not all could prove that they had a medical officer with interests and qualifications in the field of geriatrics. Three homes have now been located in each of the four metropolitan regions. In two cases houses have been purchased and are being adapted, and in four others negotiations are in train for suitable houses.

Convalescent homes enable an increased turnover of hospital patients to be made and relieve hospital waiting-lists without the heavy expense of enlarging hospitals. A survey is now being undertaken, from which it is hoped to be able to make a better assessment of the need for convalescent homes and the extent to which it is being met. The allocation of £100,000 is being distributed in large and small grants, from £50 to £10,000—small for the purchase of equipment, and large for the rehabilitation of war-deteriorated homes. Two new homes have been started—one a convalescent home for babies in Hampshire, and the other a convalescent nursery school in Sussex.

Administrative Staff College

The Fund has established in Bayswater Road a staff college for hospital administrators. It is designed to provide refresher courses for those already holding posts in the hospital service, longer courses for a limited number of young men drawn as far as possible from within the service, a continuous study of the problems and practice of hospital administration, with publication of results from time to time, and a meeting-ground for those engaged in the service. The college will be opened in the autumn of this year.

The Fund has set up a Division of Hospital Facilities which deals with requests for information and advice over a wide range of subjects. A financial advisory service is included, also a reference library, and a projected index to hospital literature. In a report on the work of the Nursing Division it is stated that there is improvement in nursing recruitment, but the demand for nurses remains unabated, particularly in certain branches. It is noted that some of the hospitals which have found it easiest to recruit nurses are taking on responsibility for beds for the chronic sick and the tuberculous, so that student nurses will undertake these branches of nursing as part of the training offered by their chosen hospital.

For six years the Fund has taken an interest in hospital catering. The Fund's advisers on this subject draw attention to the lack of trained staff in all grades. The shortage of dietitians is most acute. If only one dietitian were employed for every 150 hospital beds, 1,500 would be needed in the National Health Service, while in fact fewer than 300 are employed at the moment, and the annual output of the four training schools is barely 50.

The Emergency Bed Service of the Fund had to carry an almost unbearable load in the winter of 1948–9. As a result the service was decentralized by opening four branch offices in the London suburbs. During the winter of 1949–50, although the volume of work increased by about 20%, the speed of dealing with cases was improved; whereas it had previously taken an average of 56 minutes to arrange for the admission of a case, the time has been now reduced to 42 minutes.

The problem of long periods of waiting in the out-patient departments has been tackled by many hospitals. Most London

hospitals have instituted a full or partial appointment system, and "instances of really prolonged waiting formerly accepted as inevitable are now regarded as matters to be investigated."

Altogether, as the Report states, the hospitals are to-day on their mettle. They have witnessed more revolutionary changes in practice and outlook since July 5, 1948, than normally take place in many years.

MEDICAL BIRTHDAY HONOURS

The names of the following members of the medical profession were included in a Birthday Honours List published in *Supplements* to the *London Gazette* on June 8:

K.C.M.G.

ARTHUR ESPIE PORRITT, C.B.E., M.Ch., F.R.C.S., Chairman of the Empire Games Federation.

K.B.E. (Military Division)

CLARENCE EDWARD GREESON, C.B., M.D., Surgeon Vice-Admiral. Honorary Physician to the King.

PHILIP CLERMONT LIVINGSTON, C.B., C.B.E., A.F.C., F.R.C.S., F.R.C.S.Ed., D.P.H., D.O.M.S., Air Marshal, R.A.F. Honorary Surgeon to the King.

K.B.E. (Civil Division)

NEIL HAMILTON FAIRLEY, C.B.E., M.D., D.Sc., F.R.C.P., F.R.A.C.P., Hon.F.R.C.P.Ed., F.R.S. For services to tropical medicine.

Knighthood

ALAN NIGEL DRURY, C.B.E., M.D., F.R.S., Director of the Lister Institute of Preventive Medicine.

GEOFFREY JEFFERSON, C.B.E., M.S., F.R.C.P., F.R.C.S., F.R.S., Professor of Neurosurgery in the University of Manchester.

WILBERFORCE STEPHEN NEWTON, M.D., F.R.A.C.P. For public services in the State of Victoria.

JAMES CALVERT SPENCE, *M.C.*, M.D., F.R.C.P., Professor of Child Health in the University of Durham.

C.B. (Military Division)

WILLIAM JOHN COLBORNE, F.R.C.S., Surgeon Rear-Admiral. Honorary Surgeon to the King.

THOMAS MENZIES, O.B.E., M.B., Ch.B., D.T.M.&H., Major-General, late R.A.M.C. Honorary Physician to the King.

C.B. (Civil Division)

JOHN CECIL WILSON METHVEN, M.R.C.S., L.R.C.P. Deputy Chairman, Prison Commission.

WILLIAM REES THOMAS, M.D., F.R.C.P., D.P.M., Medical Senior Commissioner, Board of Control.

C.M.G.

WILLIAM KEVERALL MCINTYRE, *M.C.*, M.D., F.R.C.O.G. For voluntary services at the Queen Victoria Hospital and the Launceston General Hospital, Tasmania.

RICHARD LIONEL SPITTEL, C.B.E., F.R.C.S. Consulting Surgeon, General Hospital, Colombo.

WILLIAM JOHN VICKERS, M.R.C.S., L.R.C.P., D.P.H., D.T.M.&H., Colonial Medical Service. Director of Medical Services, Singapore.

C.V.O.

JOHN DOUGLAS MCLAGGAN, M.B., Ch.B., F.R.C.S., F.R.C.S.Ed.

C.B.E. (Military Division)

ABRAHAM BRISCOE, M.B., B.Ch., Air Commodore, R.A.F. Honorary Physician to the King.

WILLIAM HENRY BLINMAN BULL, O.B.E., E.D., M.B., Ch.B., F.R.C.S.Ed., Brigadier, R.N.Z.A.M.C. Honorary Surgeon to the King.

RICHARD MURPHY, M.B., B.Ch., Colonel, late R.A.M.C.

C.B.E. (Civil Division)

ARTHUR JOSEPH AMOR, M.D., M.Sc., Principal Medical Officer, Imperial Chemical Industries, Ltd.

HUGH MCINTYRE BIRCH, F.R.A.C.P., Superintendent of Mental Institutions, State of South Australia.

JAMES RALSTON KENNEDY PATERSON, *M.C.*, M.D., F.R.C.S.Ed., F.F.R., D.M.R.E., Director of the Holt Radium Institute, Manchester.

ARTHUR BUSHBY PEARSON, M.D., F.R.A.C.P., D.P.H., Pathologist to the Christchurch Hospital Board and Examiner in the Medical School at the University of Otago for many years.

CHAU SIK-NIN, M.B., B.S. For public services in Hong Kong.

O.B.E. (Military Division)

LEWIS MCKENZIE CROOKS, Ch.M., F.R.C.S., Wing Commander, R.A.F.

JOHN MACKENZIE MATHESON, M.D., F.R.C.S.Ed., M.R.C.P.Ed., Lieutenant-Colonel (temporary), R.A.M.C.

EWEN HUGH MURCHISON, M.B., Ch.B., Acting Interim Surgeon Commander, R.N.

GEORGE DESMOND WEDD, M.B., B.Chir., D.O.M.S., Surgeon Commander, R.N.

O.B.E. (Civil Division)

HENRY THOMAS CHAPMAN, L.R.C.P.&S.Ed., J.P. Member of South Melbourne City Council and Chairman of the Honorary Justices' Association, State of Victoria.

HENRY NORMAN DAVIES, M.B., Ch.B., D.T.M., Colonial Medical Service. Specialist Medical Officer, Tanganyika.

Alderman WILLIAM EDWARD MOORE EDE, M.D., J.P., Chairman of the Worcester Youth Employment Committee.

LLEWELLYN DRYSDALE INNES GRAHAM, M.B., B.Ch., D.P.H., Medical Officer to the Royal Ulster Constabulary and the Ulster Special Constabulary.

LUDWIG GUTTMANN, M.D., M.R.C.P., Neurological Surgeon in charge of the Spinal Injuries Centre at the Ministry of Pensions Hospital, Stoke Mandeville.

DANIEL LAMONT, M.B., Ch.B., F.R.C.S.Ed., Surgeon-Consultant, Gilbert Bain Memorial Hospital, Lerwick, Shetland.

GEORGE GIBSON LYTTLE, M.B., B.S., Principal Medical Officer co-ordinating civilian Medical Boards for Recruiting, Northern Ireland District.

PATINHARAM KUNNATH THALATHEL KRISHNAN NAYAR, M.B., B.S., Medical Officer, North Kedah, Federation of Malaya.

WILLIAM NORMAN AWDRY PALEY, M.R.C.S., L.R.C.P. For public services in Fiji.

MICHAEL JOSEPH PETTY, M.D., F.R.C.S. British subject resident in the Argentine Republic.

M.B.E. (Military Division)

SIDNEY FRANCIS JAYAWARDENA, E.D., M.B., B.S., Major, Ceylon Medical Corps.

M.B.E. (Civil Division)

GILBERT RASHLEIGH HULL, M.R.C.S., L.R.C.P., Admiralty Surgeon and Agent, London.

MARTHINUS HELPERUS STEYN, M.R.C.S., L.R.C.P., Medical Department, Morgenster Mission, Southern Rhodesia.

LUTHER REGINALD WYNTER, M.D., D.O.M.S., District Medical Officer, Antigua, Leeward Islands.

It is reported from the U.S.A. that two Chicago packing houses are ready to sell A.C.T.H. at the price of 100 dollars per gramme. This is a 100% reduction on the previous price, and is due to more efficient methods of manufacture. Workers at Tufts Medical College have recently developed a new technique for the rapid extraction of A.C.T.H. from dried pituitaries in powder form. They use glacial acetic acid for the extraction process, and ultra-filtration through "cellophane." With this method about 12 g. of A.C.T.H. was obtained from 100 g. of dried pituitary. A.C.T.H. prepared in this way has been given to patients in daily doses of 40 to 80 mg., which were considered to be the equivalent of 80 to 160 mg. of the preparation generally in use up to the present time. It follows that when A.C.T.H. is extracted by such methods the available supply of pituitaries should go further than at present. Another method of extracting A.C.T.H. from hog pituitaries is by an infra-red vacuum-drying process. The dried material remains as a fluffy powder which dissolves easily in water and can be used immediately.

Reports of Societies

REWRITING THE HISTORY OF MEDICINE

The Section of the History of Medicine of the Royal Society of Medicine was addressed on June 7 by Professor HENRY E. SIGERIST, who was professor and director of the Institute of the History of Medicine at Johns Hopkins University from 1932 to 1947. Dr. ASHWORTH UNDERWOOD, president of the section, was in the chair.

Professor SIGERIST said the title of his lecture, "The Need for Rewriting the History of Medicine," might appear somewhat arrogant, though he assured them that he approached the subject with profound humility. No one was more aware of the difficulties of writing a book than he who was engaged upon it. On the other hand, he would not have given up for this purpose one of the best chairs of medical history and probably its best organized department, and the comfort and security of an academic appointment, had he not been convinced that there was need for a new comprehensive history of medicine, fully documented, and following a somewhat different pattern from such works in the past.

The history of medicine had been studied for thousands of years. Ancient medicine was fully alive, its writers were regarded as authorities and sources of information, and histories of medicine were written by those who had felt the need to speculate about its origins. In the Renaissance, when there was an increasing interest in individuals, biographies of famous physicians were written, and this proved an extremely popular approach. At the end of the seventeenth or beginning of the eighteenth century a Frenchman, an Englishman, and a German each wrote a history of medicine, which was authoritative for a long time. Kurt Sprengel's *History of Medicine* (1792–1803) ran into several editions, and indeed was still interesting and worth reading. These early books set a pattern which had been followed ever since.

Scope of Historical Study

In the second half of the nineteenth century the scope of historical studies broadened considerably. It was no longer the history of wars and of treaties of peace which was written exclusively; it was also the history of human civilization, of the production of food and commodities, of social progress, of men in groups and their interpretation of the world in terms of philosophy and religion, of the conquests of science, technology, agriculture, and medicine itself, and of the recreation of the world in the form of art and literature. Into this pattern the history of medicine fitted very well, completing the picture of the history of civilization.

Classical scholars were the first to enter upon this line. The history of medicine was still a young discipline and had to catch up with other historical disciplines. In the lecturer's own generation a great deal of time had been spent in making sources available, and interpreting and translating them, but as yet there were not many centres of research. The Leipzig Institute was founded in 1905, the Institute at Baltimore in 1929, and there were a number of others not yet fully organized or productive. Most historians of his generation had received their training not in medical history itself but in neighbouring disciplines; they were physicians who had had a training in general history or in the history of art, or in Anglo-Saxon, Germanic, or Oriental studies. It was in these fields that they learned the methods which they came to apply to the study of the history of medicine.

When setting out on this gigantic task of reconstructing the past of medicine, what was it one wanted to know? One wanted to know what medicine was like at a given time and place. But this raised another question—What is medicine? To some people medicine was primarily what the physicians did, but this was obviously too narrow an approach for historical studies. Besides, who was a physician? To-day, of course, there was a legal definition. A physician was a man who had qualified from a medical school and was licensed to practise medicine. But who was the physician of antiquity—or the dentist or the nurse of antiquity? There was no licensing then, and the question was not easy to answer. The great majority of cases of illness were not seen by physicians; they were treated by the patient himself or his relatives. Self-treatment could take place in three ways: according to the principles of scientific medicine or at the dictate of commercial advertisements or by folk medicine. But it was medicine all the same, and it would be a mistake to leave this part of medical history out of the picture.

The scope of medicine had broadened tremendously in recent years, and medicine must be looked at not only as comprising what the physician did but as including the sum total of the efforts of society to promote health, prevent illness, restore health when it had broken down, and rehabilitate the sick. Such a definition implied that a history of medicine would contain far more than the doings of physicians, it would touch on the work of the educator, the statesman, the social reformer, all those who were planning and working in these fields of prevention, treatment, and care.

Therefore when the investigation of the history of medicine began it was necessary to start with a study of the health conditions of a given society at a given time, its incidence of illness, its prevailing diseases, and whether its people were long-lived or short-lived. The state of health was determined to a large extent by geographical and economic factors. There was the hereditary factor also, which was difficult to approach historically, but the physical and social environment could be studied, and the work and habits and life of the people generally, determining their physical and mental health. Housing, nutrition, labour conditions, rest, and recreation were all factors which it was necessary to consider.

Then it was important to know what was done when health broke down—the use of magic in some communities, the prohibition of certain foods, the prescription of drugs, the employment of physical and surgical methods. The historian must forget his present theories and make himself a naive observer, endeavouring to find what such an observer, unembarrassed by later theories, would see and would think about what he saw. Medical theories were one aspect of the general civilization of the times, and to understand them it was necessary to have regard to many things—to the religion, the law, the music, the art of the period, especially art, because the sensitive artist was able to express the new trends spontaneously, and usually did so long before the scientist.

Rank and File Doctors

The importance of the individual in the history of medicine, Professor Sigerist went on, must not be forgotten. There were in the history of medicine doctors who were acknowledged to be great, not because they were primarily great scientists, but because they so nearly fulfilled the medical ideals of their time. Highly important in the history of medicine was the job of the general practitioner—the rank and file doctor. It was important for a country to have great medical scientists, and the pioneers who did basic work in the hospitals and laboratories, but it was equally important to have a high standard among the general practitioners, who would apply the discoveries of the scientist for the benefit of the patient. Therefore the history of medicine would have to pay great attention to the work of the rank and file doctor and his auxiliaries. Medicine was not a natural science, either pure or applied; it was primarily a social science and its goal was social—namely, to readjust men to society or to maintain their adjustment.

It was not enough, therefore, to study what the leading workers had thought and achieved; the social history of the patient, of the physician also, and of both in their mutual relationship must be studied. The position of the patient had changed a great deal in the course of time. It was different in every society, and the challenge to medicine was different in a society which took no interest in the patient and let him die if he could not afford a physician, and the society which felt a strong responsibility towards its sick members. As for the physician himself, it made all the difference whether he was a

sorcerer, a craftsman, a cleric, or a scientific social worker. His position in society, his training, the organization of his practice, the doctor–patient relationship, the measures which a society might take to protect itself against the undue power of the physician were all germane. From ancient times there had been control of the physician by codes of ethics, Hippocratic oaths, societies, and the like. For a long time the relationship between physician and patient was regarded as private, but medicine had become more and more integrated with social institutions, and the question of national health insurance and national health service was obviously part of the history of medicine.

In some closing remarks on the mission of the historian, Professor Sigerist said that the historian sought for sources, analysed and interpreted them, reviewed what he had found, and put it together, so that gradually he assembled a picture of the past which in a sense became alive. The synthesis first took place in the historian himself; it was a great experience for him, and he wanted to share it with others. What he had discovered in his researches he now had to formulate. The writing of a historical book was a creative process and an artistic process. The historian, of course, could not create freely as the poet could; his methods of research imposed an iron discipline upon his imagination. Nevertheless, it was his experience which he was writing down and passing on to his fellow men. Much, therefore, depended on the personality of the historian.

Medical history was one approach to the problems of medicine. The historian, while serving the truth in his history, was at the same time endeavouring to contribute his share to the progress of medicine, and the book he wrote, fully documented, would be not only a synthesis of the past but a starting-point for further research.

A cordial vote of thanks to Professor Sigerist was carried on the motion of Dr. JOSEPH NEEDHAM, seconded by Professor BENJAMIN FARRINGTON.

POLIOMYELITIS

RECENT SYMPOSIUM

The Fever Hospital Medical Services Group of the Society of Medical Officers of Health held a two-day symposium on poliomyelitis at the Western Hospital, London, on May 19 and 20 under the chairmanship of Dr. E. G. BENN, the president of the Group.

Dr. W. H. BRADLEY (Ministry of Health), discussing the epidemiology of poliomyelitis, pointed out that the disease had suddenly become pre-eminent in the field of communicable diseases in this country. The first real epidemic in Great Britain occurred in 1947 when the attack rate in England and Wales was 18 per 100,000 living, which was four-and-a-half times as great as the 1938 high figure and comparable with the rates recorded in the U.S.A. in 1916 and in 1946. In 1947 there were three times as many deaths as in 1938, but the case fatality rate was only 9% compared with 16% in 1938. The age distribution showed the upward trend characteristic of recent epidemics in civilized countries; 55% of the deaths registered were in persons over 15 years of age. The geographical distribution showed a departure from the former rural preponderance, and there was evidence of spread into the rural areas from the cities. The epidemic began in a number of widely separated places at about the same time, but not necessarily simultaneously. In these places some warning of the impending autumnal epidemic was given by a higher incidence than usual at the beginning of the year. There was some evidence of concentric spread from these centres in the early stages, but this was soon lost in the general spread.

In 1948 there was a "hangover" from 1947, and a similar effect appeared in 1950 after the 1949 epidemic, which was second only to the 1947 one. The epidemic of 1949 began a little later than that of 1947 but was more prolonged. In 1947 the peak weekly figure of 708 cases was reached in the thirty-sixth week of the year; in 1949 the figure was 463 and occurred in the forty-third week. The whole country was involved in both epidemics; it was not the general rule that areas lightly attacked in 1947 were heavily attacked in 1949. Useful information about the epidemiology of poliomyelitis was provided by the Jersey outbreak in 1948. The island escaped in 1947 despite many visitors from Great Britain. The outbreak suggested a harbinger case, the survival of infection in the area, and a subsequent outbreak.

Discussing poliomyelitis occurring after injections, Dr. Bradley said the Ministry had been receiving reports for some years of the complications of immunization. Professor Bradford Hill had conducted a statistical inquiry for the Ministry and had found an undoubted association between recent inoculation and paralysis affecting the injected limb; the finding was most evident with A.P.T.–pertussis vaccine, less so with A.P.T., and the figures for pertussis vaccine alone were inadequate for drawing conclusions. The risk of poliomyelitis after injections had not yet been determined, but some idea could be obtained from a report that among 1,453 cases of poliomyelitis in the age group 0–4 there were 26 cases of recent inoculations, not all of which could be regarded as responsible. The task of obtaining reliable information was formidable and required controlled investigation. Off-season immunization might be desirable for nurses in fever hospitals and subcutaneous injections might be safer than intramuscular, but immunization should not be discouraged except in the locality of an epidemic.

Dr. Bradley also reported 12 examples in one year of cross-infection with poliomyelitis in hospitals which, with one exception, were general hospitals. The power of the disease to spread directly merited more respect than it had received in the past.

Australian Experience

Dr. B. P. MCCLOSKEY (Melbourne, Australia) reported that during the routine investigation of poliomyelitis in Victoria, Australia, attention was directed to cases following inoculation. The conclusions reached were that in Victoria during 1949 recent inoculation with pertussis vaccine, either alone or in combination, was associated with the onset of paralytic poliomyelitis; that the mean interval between such an inoculation and the onset of poliomyelitis corresponded with the presumed incubation period of poliomyelitis; further, that the actual number of cases of paralytic poliomyelitis occurring was increased by the administration of inoculations during the currency of this epidemic. Also the severity of paralysis in cases with a history of recent inoculation of pertussis vaccine, either alone or in combination, was significantly greater than in those with no such history. The evidence that recent inoculation with diphtheria prophylactic was associated with the onset of paralytic poliomyelitis in Victoria during 1949 was much less conclusive, although it was not so inconclusive as to be a purely random finding.

The difference between the findings in Great Britain, where the evidence against diphtheria immunization was strong and that against pertussis vaccine weak, might be explained by the fact that in Australia diphtheria prophylactics were given subcutaneously and with little local reaction, whereas pertussis vaccine was given intramuscularly and was commonly followed by reaction. In Great Britain A.P.T. was the common prophylactic and was given intramuscularly.

"Bulbar" Poliomyelitis

Dr. W. HOWLETT KELLEHER (London) said that, strictly speaking, "bulbar" poliomyelitis involved only the medulla, but the term commonly included involvement of the brain stem. In polio-encephalitis spasticity and other symptoms had been attributed to damage to the brain stem, although cerebral hypoxia might be responsible for some of them. The incidence and severity of bulbar lesions varied. In 1947 the proportion of cases was higher but the severity was less than in 1949. The Minnesota Research Commission had classified "bulbar" poliomyelitis into: (1) the cranial nuclei group; (2) the respiratory centre group; (3) the circulatory centre group; and (4) the encephalitic group.

Combinations of these groups were seen, and the first group could be subdivided into upper and lower subgroups. Palsies of the upper cranial nerves (fifth, seventh, and eighth) were common and mild in 1947 and they gave rise to little anxiety.

Involvement of the lower cranial nerves, particularly damage to the nucleus of the tenth cranial nerve, was associated with the dangerous features of bulbar poliomyelitis, and was prominent in 1949.

Involvement of the respiratory centre was difficult to recognize clinically, although histological evidence of such involvement was common. Some of the symptoms had been ascribed to hypoxia. Involvement of the circulatory centre was not recognized in any of Dr. Kelleher's cases. Encephalitic symptoms were exceedingly common, but here again hypoxia might be responsible. The whole problem of bulbar poliomyelitis appeared to be concerned intimately with defects of oxygen concentration. By contrast with poliomyelitis, laryngeal diphtheria necessitating tracheotomy did not appear to cause post-anoxic cerebral damage. Factors which added to the anoxia were pooling of pharyngeal secretions, reflex laryngeal spasm from the aspiration of small quantities of secretion, abductor paralysis of the larynx, pulmonary atelectasis, pneumonia, and pulmonary oedema. The first three might cause rapid asphyxia.

Drugs, antisera, and antibiotics were not effective against poliomyelitis. Curare had been used to relax muscles in spasm and this seemed to be a rational procedure. Hot compresses alleviated the tight respiratory muscles. Intravenous glucose had been used for cerebral dehydration. Sedatives had their uses and dangers. Nasal feeding must be used with the greatest caution, for collapse and death had followed nasal feeds. Oxygen therapy was clearly indicated in selected cases, but the airway must be kept free. For this purpose postural drainage, intermittent or continuous pharyngeal aspiration, and intratracheal aspiration were employed. In the supine position a degree of tilt for drainage as great as 45 degrees might be required; in the prone position the angle was reduced.

Tracheotomy should be a carefully planned operation, not an emergency one. To those who favoured it there were many indications for its early performance; indeed some claimed that it was essential before treatment in a respirator in order to ensure a clear airway. The team treating cases of poliomyelitis should include an anaesthetist and a laryngologist. Tracheotomy was sometimes carried out with a bronchoscope or endotracheal tube in place. A high tracheotomy allowed subsequent nursing in a respirator. The Stille and the Moynihan collarless respirators had advantages in this type of case. Positive pressure oxygen therapy was required if there was any suspicion of pulmonary oedema. To all these measures, however, the group with involvement of the respiratory centre or of the circulatory centre responded poorly.

Use of Respirators

Dr. RITCHIE RUSSELL (Oxford) reported on an investigation at the Western Hospital by his small research group, consisting of Dr. Margaret Taylor and Dr. Eleanor Davies-Jones, in collaboration with Dr. R. B. Bourdillon of the Medical Research Council. Discussing the use of respirators in poliomyelitis, he said that life in a respirator was highly precarious, yet decisions had to be made on criteria which were rough and inexact. Consequently decisions were often deferred until severe anoxia had developed. Dependence was usually placed on the extent of the chest movements, the patient's colour, and the sound and strength of the cough. Dr. Kelleher determined how many the patient could count in one breath. All these tests were crude.

Correct speeds and pressures in the respirator were difficult to assess. Over-ventilation developed insidiously and might be as disastrous as under-ventilation. An easy method of recording tidal air and vital capacity was an urgent requirement, not only for deciding on the need for the respirator but for determining its efficacy in use. In the study undertaken by the team a recording spirometer was used. For research purposes the study of the alveolar CO_2 was also required. What was needed was a comprehensive study, including a follow-up of cases treated in respirators. When breathing became difficult the patient's anxiety influenced the decision whether to use a respirator. He suggested for consideration the administration at this stage of a strong sedative. The difficulty was to decide which was safe; any sedative which caused vomiting was dangerous and might cause death. Experimental study in animals was needed. For postural drainage in the respirator the prone position with frequent changes of posture was worth further trial because a good tidal air could be obtained in this position. Support for the patient and a better neck seal were required. Other improvements in respirator design suggested were accurate pressure and temperature control, a quick method of tilting, an alarm system to indicate failure of pressure and adequate ports for nursing and for setting up intravenous transfusion and bood-pressure recording apparatus. With every respirator it was desirable to have a lung inflator or, better, a suck–blow machine which would maintain respiration adequately when the patient was temporarily removed from the respirator. Inquiry was also needed on the best method for weaning the patient from the respirator.

Dr. R. B. BOURDILLON (Medical Research Council) said that it was possible to obtain a rough measurement of breathing by using an anaesthetist's bag and elephant tubing. He demonstrated a simple improvised bellows for providing a rough idea of a fading vital capacity; for tidal air a similar but smaller bellows could be used. Tidal air should never exceed 600 ml., preferably not more than 500 ml.; a litre involved over-breathing. Among the dangers of over-ventilation were cerebral anoxaemia from constriction of the cerebral vessels.

Treatment after the Acute Stage

Dr. C. D. S. AGASSIZ (Carshalton) read the first of three papers on the treatment of anterior poliomyelitis after the acute stage. Cases were now accepted for physiotherapy as soon as possible after the painful phase. He was impressed by the better condition of those who had received hot packs and by the unsatisfactory "tightness" of those patients who had been immobilized in splints or plaster casts.

The child was nursed flat in bed with a firm mattress or bed-board and with a footboard. A simple form of restrainer was necessary to prevent the child sitting up. In the prevention of deformities attention must be directed not only to paralysis but to "tightness" which interfered with the functions of the underlying muscles. Failing hot packs the affected limbs were sprayed alternately with hot and cold water until the skin was flushed. The patient then lay in a bath of warm water for ten to fifteen minutes, and was dried before physiotherapy was started. Passive movement was restricted by "tightness," which was gradually overcome by regular stretching short of the production of pain. Instruction by the physiotherapist in muscle movements was carried out and when the child's feet could be brought to a right angle he was made to stand, with support. Re-education in walking then began. Elbow crutches were preferred to arm crutches, and by prolonged re-education of the type described a patient with complete flaccid paralysis of both lower limbs could walk with sticks. Callipers were a last resort. He attributed the increase in the number of cases needing such appliances in 1949 to the development of a waiting-list for admission to hospital. Instruction to parents and attendance at aftercare clinics were both essential.

Mr. R. H. METCALFE (Carshalton) supported Sister Kenny's views on pathology and on therapy. Poliomyelitis was not the localized disease it was formerly thought to be. Not only nerves were involved but nerve end-plates, muscles, fascia, and skin, which became tight and needed to be stretched. Splinting was to be condemned and is probably responsible for shortening. Moist heat and stretching relieved "tightness." He demonstrated tests for "tightness" and for muscle power and methods of recording on muscle charts. He stressed the importance of the mental outlook—the enthusiasm and optimism of the patients and of the staff.

Mr. A. ROCYN JONES (London) discussed occupational therapy, rehabilitation, and the ultimate fate of patients with poliomyelitis. The orthopaedic surgeon must collaborate with the physician from the beginning. As soon as patients were fit their muscles must be trained for an occupation. In children education must be arranged, as they might be in hospital for eighteen months to two years. Occupational therapy had two advantages: it encouraged muscles which were recovering and

directed the patient's attention away from his disability, thus preventing periods of depression. In both physiotherapy and occupational therapy fatigue in recovering muscles must be avoided and patients must be handled gently. Grading of activity according to the capacity of the muscles was therefore essential.

Two types of occupational therapy were particularly suitable in poliomyelitis—modelling and weaving. At the end of eighteen months to two years the permanent disability could be assessed and a decision made whether any operation or appliance would help. If possible callipers should be avoided. The basic operation was arthrodesis; tendon transplantation gave disappointing results. In the rehabilitation of children leaving hospital ordinary schools were to be preferred to schools for the physically defective if practicable. Emphasis should be on the patient's capacity, not his incapacity. On leaving hospital 80% of patients were capable of learning a remunerative occupation. In training schools young patients (16 to 21) should be grouped together and not mixed with adults disabled in industry. Training for some industries might take three years, after which the recovered patients could often compete with the able-bodied worker.

ANIMAL DISEASES INIMICAL TO MAN

A joint meeting of the Midland Medical Society and the Midland Veterinary Medical Association took place on April 19 at the Birmingham Medical Institute. Mr. BARON T. ROSE reminded those present that the last joint meeting of this kind was held in 1933. Mr. J. S. M. CONNELL then opened the discussion on the subject: "The Importance to the Community of the Control of Animal Diseases Inimical to Man."

Mr. WALTER SCOTT, F.R.C.V.S., said they were all concerned with tuberculosis, but the man in the street was more conversant with what the medical profession was doing to combat tuberculosis than with what the veterinary profession was doing. Comparatively few people knew about the Tuberculosis (Attested Herds) Scheme, and yet under this scheme, at the end of 1949, there were 44,889 herds in the country, comprising 1,762,200 cattle which were officially certified to be free from tuberculosis. That represented a figure of 19.0% in an adult population of over 9 millions. Mr. Scott reminded his listeners that, while cattle could and did infect man with tuberculosis, it had been known for man to infect cattle. On the subject of anthrax he said that there had been a marked decrease in the number of cases confirmed among cattle in this country during the last few months.

Mr. Scott finally emphasized the necessity for the rigid enforcement of the six months' quarantine period for any dog or cat entering this country from abroad. Since November, 1946, nine cases of rabies in dogs had been confirmed in quarantine stations. He pointed out the risks to which dogs and people would have been exposed had the affected animals not been in quarantine.

Mr. F. CHAMBERS, F.R.C.V.S., said that the domestication of animals, resulting in a close relationship with man, had created important medical problems. The medical and veterinary professions must co-operate more closely if headway was to be made in controlling or even eradicating certain diseases in man.

Brucellosis, leptospirosis, tularaemia, the variolas, scabies, and some diseases caused by fungi were all communicable to man. During recent years many papers had appeared in the scientific press on the transmission of *Brucella abortus* to man. Brucellosis was one of the chief causes of contagious abortion in cattle, and once the infection had been introduced into a clean or non-inoculated herd it spread with great rapidity, causing 70 to 80% of the cows to abort about the seventh month of pregnancy. The placenta was nearly always retained, with unpleasant consequences. There were three well-defined species: *Br. abortus, Br. melitensis,* and *Br. suis.* The last, which caused abortion in pigs, had not been detected in this country. The three species were too closely allied to be separated by ordinary agglutination tests.

Goats did not appear to harbour *Br. abortus,* and so far as this country was concerned it would seem that the consumption of goat's milk could be encouraged without undue risk. After going into the subject of brucellosis in some detail, the speaker remarked that it was Llewellyn Bevan, the veterinary bacteriologist in Southern Rhodesia, who showed that blood from a man in Salisbury Hospital agglutinated *Br. abortus* in a dilution of 1:200. Veterinarians were far more liable to infection than members of any other occupational group in close contact with domestic animals. Medical men practising in country districts were familiar with allergic reactions on the arms of those who came into close contact with animals infected with *Br. abortus.* Unfortunately, although a cow might not abort, it might be a carrier, and in a small proportion of cases *Br. abortus* was excreted in the milk. The culprit could be found only by testing every cow in the herd. If a case was found during the routine sampling of milk the producer must have all the milk heat-treated before sale. This seemed to be a reasonable preventive measure, but it did at times cause inconvenience and expense, especially if the owner was a producer-retailer.

The relative infrequency of clinical undulant fever in persons exposed to the risk of infection was explicable on one or both of the following grounds: (1) that the organism had only a low degree of virulence and was incapable of infecting humans unless their resistance was unduly lowered; (2) that only a small minority of strains were of sufficient virulence to invade the body.

Discussing leptospirosis, he said this was a disease mainly confined to the dog, although cases had been described in the horse, and recently there had been large outbreaks in cattle in the U.S.A. The source of infection in man was usually the rat. In the dog the usual organism was *L. canicola,* but the very acute cases might be due to *L. icterohaemorrhagiae.* Dogs caught the infection by sniffing where rats had urinated or by eating from vessels soiled by rat urine. In this country it was said that 30% of rats harboured the parasite without much harm to themselves. In 1948 Molnux showed that 55% of rats in New York had leptospires in the kidneys; 23% of farm rats and 66% of dump rats harboured leptospires.

Swine erysipelas would also attack man, and the chief victims were veterinary surgeons and those employed in abattoirs who handled sick animals or the carcasses of infected animals. Those in charge of meat inspection also had to watch for cysticercus infection.

In the ensuing discussion different speakers mentioned actinomycosis, anthrax, and histoplasmosis. In his reply Mr. Chambers mentioned that many problems of veterinary pathology might have similar counterparts in human medicine—for example, "scours" in small unweaned pigs. It was also noticeable that a recent increase in the incidence of tuberculosis in man might be associated with the recent large increase of tuberculosis-free herds. It was possible that the population was being deprived of a means of naturally acquiring immunity to tuberculosis.

NUTRITION SOCIETY

RECENT EXPERIMENTAL WORK

A meeting of the Nutrition Society for the communication of miscellaneous papers was held on May 27 at the London School of Hygiene and Tropical Medicine. Dr. J. HAMMOND, F.R.S., presided at the morning session and Professor R. C. GARRY during the afternoon.

K. J. CARPENTER and J. DUCKWORTH described an investigation of the value of vitamin B_{12} as a supplement for poultry receiving the rations usually given in this country. Preparations of this vitamin derived from fermentation products or fish concentrates have been used successfully in America to improve diets containing vegetable sources of protein, such as soya bean meal, but no benefit was obtained with British rations containing fish meal.

E. R. BRANSBY and H. HAMMOND discussed the complicated factors which influence the growth of children, with particular

reference to the difficulties involved in using measurements of height and weight as a guide to nutritional status. Divergent conclusions might be drawn according to whether measurements were compared simply with the age of the child or with the rate of increase over a preceding period. Allowances had to be made for the different ranges of normality in children of slender or of stocky build, and heights measured sitting and standing might lead to different conclusions. When all the appropriate formulae relating age, height, weight, gain in weight, and body configuration had been applied and summarized the examiner still had to decide how far the child's growth had been influenced by nutrition, as compared with general health, economic position, and housing. In better-class homes children tended to be taller than in poorer homes, but less fat.

G. H. BOURNE reported preliminary experiments in which he had detected abnormalities in the islets of Langerhans of guinea-pigs deprived of vitamin P. The average blood sugar in a group of affected animals was somewhat higher than in control animals, and the highest levels of blood sugar tended to be associated with the most severe histological lesions. A diet deficient in the "anti-stiffness" factor also affected the islets of Langerhans, producing considerable hypertrophy. The freedom of Panama natives from diabetes, as compared with the Spanish inhabitants of the same region, might conceivably be due to their consumption of the "anti-stiffness" factor in the form of crude sugar-cane products.

V. RAMALINGASWAMI and H. M. SINCLAIR described and demonstrated the lesions of the muco-cutaneous junctions produced in rats deficient in pyridoxin. Redness and loss of hair were observed at the lips and anus, with acanthosis and hyperkeratosis. The paws also became scaly. The primary disturbance appeared to be one affecting the vascular system.

Vitamin B_1

D. E. TRIBE, J. G. GORDON, and J. WHITFIELD gave an interesting account of experiments in which rats were allowed to choose between diets adequate and defective in vitamin B_1. The animals succeeded in selecting the diet containing the vitamin, although human volunteers failed to distinguish between the two diets by their appearance, taste, odour, or texture. The authors agreed with Harris's conclusion that the rat must derive some feeling of well-being which it associates with the vitaminized diet. In their experience, however, it was unnecessary to provide a "marker" for the vitamin by associating it with a distinctive flavour, at least as judged by human standards. Presumably the rats were able to taste or smell the vitamin in concentrations too low for detection by humans.

H. E. MAGEE and E. M. H. MILLIGAN summarized their extensive studies of haemoglobin levels in pregnant and lactating women. During the first trimester of pregnancy values were 89–95% of normal, during the second 86–90%, and during the third 82–85%. Haemoglobin levels rose after parturition, but only reached 90% after 60 weeks. Iron therapy was effective in raising the haemoglobin concentration both before and after parturition.

Nicotinamide Deficiency

L. J. HARRIS and E. KODICEK outlined their studies on nicotinamide deficiency in rats. This animal was for a long time considered to be useless for the purpose of estimating nicotinamide, since when given basal diets containing adequate amounts of protein it fails to show any of the signs of nicotinamide deficiency. This immunity could readily be explained by the production of nicotinamide from tryptophan, and it appeared possible that deficiency might be induced by depriving the animal of nicotinamide and at the same time greatly reducing the protein allowance. The rat is so resistant to nicotinamide deficiency, however, that even a diet consisting mainly of maize produced no lesions, but a diet in which maize, with a little casein, was diluted with sugar regularly caused fatal nicotinamide deficiency. Graded doses of nicotinamide, or doses of tryptophan 40 times larger, produced correspondingly graded growth responses. In testing foodstuffs which contain both nicotinamide and tryptophan the method did not distinguish between these substances, but gave a total value representing their combined activities.

G. H. BOURNE and L. J. HARRIS then described the histological changes in rats deficient in nicotinamide. Abnormalities were observed in the intestinal walls, and particularly in the oxyntic cells of the stomach. The spleen was reduced in size, and there was a loss of staining ability in the anterior pituitary gland. Lesions of the kidney tubule were also prominent, but were observed even in animals treated with nicotinamide. Further experiments to eliminate the effects of inanition are now in progress.

W. T. C. BERRY and P. J. COWIN found that in clinical examinations no reliable relation could be traced between the colour of the gums and the haemoglobin level of the blood. T. MOORE displayed photographs of the incisor teeth of albino and piebald rats deficient in vitamin E, and demonstrated that the brown pigment which normally covers their anterior surfaces was lost much more readily in the albinos than in the piebalds. R. ASCHAFFENBERG, S. BARTLETT, S. K. KON, J. H. B. ROY, D. M. WALKER, C. BRIGGS, and R. LOVELL reported progress in their investigation of the factor present in bovine colostrum which is responsible for the survival of, and prevention of diarrhoea in, newborn calves. A globulin derived from the whey was found to be effective when given orally in small amounts.

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

At a meeting of the North of England Obstetrical and Gynaecological Society held in Leeds on April 28, the president, Mr. H. HARVEY EVERS, was in the chair.

Mr. J. B. COCHRANE described a case of calcified ovarian fibroma in a girl of 15 who had complained of irregular painful menstruation associated with menorrhagia. She was found to have a stony-hard tumour of the left ovary. The uterus was normal, but four tiny nodules were discovered attached to the right ovary.

Dr. E. E. RAWLINGS read a note on a case of multiple calculi in the female urethra. His patient was an obese woman of 60 who was a diabetic and had complained of stress incontinence; there had also been dysuria. A curious swelling was felt in the suburethral region and crepitus was elicited. An incision was made into the floor of the urethra and three calculi were removed. The patient had recovered perfectly well from the operation and there was no leakage of urine.

Meigs's Syndrome

Mr. H. R. ARTHUR described a case of Meigs's syndrome with a thecoma in a woman of 59. She had a right-sided pleural effusion and had first of all been treated in the medical wards. In addition to the pleural fluid there was an ovarian tumour with gross ascites. When the abdomen was opened a large necrotic ovarian tumour was discovered, and at the time it was thought to be malignant. The only odd feature was that the other ovary seemed perfectly normal. Subtotal hysterectomy and removal of both appendages were carried out. Laboratory examination showed that the tumour was a benign thecoma.

In conclusion, Mr. BRYAN WILLIAMS read a paper on neonatal deaths following caesarean section, and described a syndrome in which babies delivered by section appeared perfectly all right at first but developed attacks of apnoea and blueness some hours afterwards and often succumbed. He suggested that catheterization of the respiratory passages should be carried out and gastric aspiration should also be considered. He drew attention to the high foetal mortality following caesarean section, and an interesting discussion followed.

A pamphlet describing spas in Italy is obtainable free on request from the Italian State Tourist Department, Kendall House, 1, Conduit Street, London, W.1.

Correspondence

A New Method of Bronchography

SIR,—In reply to Professor R. R. Macintosh and Dr. W. W. Mushin (June 3, p. 1319), we would like to stress that from the outset it was obvious that the method of concentric tubes would be of no value for bronchography in children, because the essentially small bore of the inner tube would be unsuitable for the introduction of viscous "lipiodol." Collaboration between the paediatric and anaesthetic units in our group has evolved the following procedure for use in children from the age of 2 years and upwards.

We employ a solution of 5% thiopentone containing 80 mg. of "flaxedil" to 20 ml. of this solution. Venepuncture is readily accomplished by using a ½ in. 20 gauge needle, and 1 ml. is given for each year of age. Oral intubation is performed under direct vision, using a small endotracheal tube the external end of which is controlled by thread passed through the rubber wall. The child is then positioned, and lipiodol introduced. When filling of the appropriate bronchi has been accomplished the tube is withdrawn. Smooth respiration of controlled depth can be maintained throughout roentgenography by a cyclopropane-oxygen mixture administered through a mask and Cope's absorber.

The advantages of this method are: (1) the ease of filling appropriate lobes before photography and of controlling respiratory movements throughout this procedure; (2) the time-saving factor, which is greatly appreciated by the busy radiodiagnostic department of the present day (the average time for the procedure from start to finish is eight minutes); and (3) the reduction to minimal proportions of systemic disturbance and psychic trauma to the child. Using this method we have never failed to obtain an effective bronchogram for radiodiagnosis, and children have been able to return home on the same day. In our opinion, the use of topical anaesthesia for bronchography in children is unnecessary and not without risk.—We are, etc.,

W. R. SPACEK.
E. A. J. BYRNE.

Royal Lancaster Infirmary, Lancaster.

SIR,—The correspondence on methods of bronchography in the columns of the *Journal* prompts me to describe a technique which I have recently adopted.

A cuffed endotracheal tube of appropriate size is chosen, and the tube is cut obliquely just proximal to the cuff, so that the small inflation tube lies at the tip of the new bevel. The endotracheal tube is introduced under general anaesthesia and is manipulated into the appropriate main bronchus. Anaesthesia is maintained with nitrous oxide and trichorethylene, using Ayre's T-piece. The iodized poppy-seed oil is introduced through the inflation tube, the pilot balloon having first been removed, and is thus concentrated on the appropriate side. In order to facilitate injection through the rather small tube the oil should be warmed to blood heat.

This method can be used satisfactorily without passing the endotracheal tube beyond the trachea should this be preferred. By this means the advantage of endotracheal anaesthesia is combined with a technique which does not limit the size of the airway.—I am, etc.,

Newcastle-upon-Tyne. M. H. ARMSTRONG DAVISON.

Morphine in Status Asthmaticus

SIR,—The recent correspondence in the *Journal* has rightly emphasized the dangers of giving morphine in bronchial asthma in cases complicated by bronchitis. Other contraindications are that morphine should not be given in bronchial asthma except as a last resource in status asthmaticus, that it should always be combined with atropine (1/75 gr. = 0.9 mg.), that a second dose of morphine should never be given until the full effects of the first have ceased to act, and that the drug should be discontinued at the earliest possible moment.

Adrenaline 1 in 1,000 by subcutaneous injection or aminophylline intravenously should be given for status asthmaticus in adequate doses, repeated as necessary, before morphine is considered. To combat the exhaustion and cyanosis of status asthmaticus oxygen inhalations are valuable, and glucose drinks should be freely given, especially when repeated injections of adrenaline are necessary. When these and other remedies are ceasing to give relief morphine 1/6 gr. (11 mg.) or ¼ gr. (16 mg.) of morphine with atropine (1/75 gr.) will usually relieve the vicious circle of sleeplessness, exhaustion, and the struggle to breathe, and allow adrenaline or aminophylline again to prove effective. It is true that fatalities have been reported after the use of morphine in status asthmaticus, as also after the use of antihistaminics and aminophylline. Patients do die in status asthmaticus, especially if they are inhaler users. Benson and Perlman,[1] in a survey of a large number of cases over a ten-year period, found the death rate as a direct result of asthma was five time as high in habitual inhaler users as in other asthma cases. Yet each of the above remedies has its place in asthma.

I know of a case of status asthmaticus which proved fatal after morphine was given when the patient was all but moribund. This patient might have lived had morphine been given earlier. The late George Bray, who had a vast experience of bronchial asthma, considered that morphine ¼ gr. with atropine 1/75 gr. and 10 minims (0.6 ml.) of adrenaline (1 in 1,000), given slowly subcutaneously at the rate of 1 minim every fifth minute—one minim of adrenaline 1 in 1,000 being given subcutaneously from another hypodermic syringe each intervening minute until the asthma was relieved or the dose of morphine completed—was an invaluable remedy in status asthmaticus.[2]

My experience has been that morphine should be given only as a last resource, but its administration should then be not too long delayed.—I am, etc.,

London, W.1. CLEMENT FRANCIS.

REFERENCES
[1] *J. Allergy*, 1948, **19**, 129.
[2] *Recent Advances in Allergy*, 1937, London.

The Training of the G.P.

SIR,—I have read the summary of the B.M.A. Committee's report, *General Practice and the Training of the General Practitioner* (May 27, p. 1251), with increasing alarm and despondency. What I want to ask is, Is your planning really necessary? The first thing that strikes one is this: That for years we have been told we are "the backbone of the profession"—the "front-line troops." We are the blue-eyed boys, and now, in the same breath, we are informed that our training has, presumably, been woefully inadequate for this vital job, and that drastic steps are recommended to deal with this appalling state of affairs. What has been so wrong with "the standards and status of general practice" over the years? The answer is surely, "Very little."

Those of us who are now nearer 50 than 40 can remember three or four generations of practitioners. There was the G.P. of our boyhood days. With the paucity of the shots in his therapeutic locker he did a grand job of work. He was respected and liked, with few exceptions, wherever he went. He had a high standard of ethics and honour. He handed down great traditions. Would he have been any better, I wonder, if the planners had compelled him to train for a further three years after having obtained the necessary degrees sanctioned by Parliament?

Take the generation preceding my own. Thousands went to the 1914 war, where they served with gallantry. They, now in their late fifties or middle sixties, have been in practice ever since. I know dozens of these men. I was helped and encouraged by them when I went into practice as a very young doctor. I know of no finer type than this particular crowd. Would their "standing and status" have been improved, I wonder, if the planners had got their claws on them 30 years ago?

Myself and my contemporaries, what did we do? Much the same as our predecessors. After doing a house job or locums—if we wanted to, of our own free will as free men—we went into practice when we liked. Have our standards been so very low? Has there been any public outcry about our deficiencies? Why should our sons be any less competent after qualifying? Why should they be forced to attend lectures which include such a fatuous subject as how to obtain the district nurse? Cannot the planners realize that a good G.P. like a good officer

is born and not manufactured? He learns by experience, yes, but if he has not got that *je ne sais quoi* he will never make the grade. This is borne out by the numbers of one's fellow-students who fell by the wayside. The sorting out process begins very early; and how, if they cannot fit into practice, will another three years (including lectures on the regulations of the N.H.S.) be of benefit?

There is one "function and responsibility" undertaken by the general practitioner which the young G.P. will avoid like the plague. Whom Sally should marry, upon what income, is not the doctor's business. I have had some. If I say "yes" and things go wrong, Sally, her parents, brothers and sisters, bridesmaids, and best man go off my list forthwith. If I say "no," Sally has a nervous breakdown, I get a night call, and the boy friend glowers at me at the village cricket match. For sixteen bob a year it is not worth it.

Finally, Sir, is not this lust for "planning"—which even goes so far as to tell us what books we should read in our spare time—which has now unhappily invaded the art and science of medicine, just one other frightening example of the universal desire to pry into one's neighbour's back garden and organize his private affairs?—I am, etc.,

Aylesbury, Bucks. W. A. BELLAMY.

SIR,—Compulsion and regimentation rule our lives in ever increasing degree, but no section of the community seems more eager to put a rope round its own neck than the medical profession. Many of the present generation of medical students look with despair upon the insidious loss of professional freedom manifest in recent years and upon the feeble efforts of the leaders of the profession (with certain exceptions) to stem the tide.

In the Medical Bill, soon to come before the House of Commons, it is proposed that on qualifying doctors should be enforced to work for one year in resident hospital posts before full registration. Surely the majority always have been and always will be only too glad to avail themselves of this extra experience. This Bill, then, will only produce a minority of resentful house officers, who will in consequence benefit little from their duties.

The latest threat to professional freedom again comes from within the profession, in the report *General Practice and the Training of the General Practitioner* (May 27, p. 1251). This report from the committee under the chairmanship of Sir Henry Cohen contains recommendations which, if not opposed by the profession, will almost certainly become law in the near future. This committee feels that the prospective general practitioner should serve three years after registration before he is entitled to work in the career of his choice. It will take 5½ years to qualify, one year residency, and three years' postgraduate work—i.e., 9½ years' study—before he is allowed to settle down to practise. He is 28½ years of age before he assumes any real responsibility. What a dreary prospect.

Few would deny that a preliminary assistantship is of the greatest value to the young practitioner. He is guided by and able to consult his experienced principal. There is, then, little quarrel with the proposal for the trainee's first year; but, because it is almost impossible these days to enter general practice without a preliminary assistantship, there is no need for this compulsion. The second year of his training would be spent in hospital, "not to increase the trainee's knowledge of rare diseases but . . . to recognize where specialist help should be sought." One might think that the trainee had learned nothing during his three years' clinical studentship, one year as a resident, and one year as an assistant. The poor man might even think that it would be better if he remained with the principal gaining more experience of general practice rather than being exported and sent off to some hospital. The third year is again to be spent in hospital.

The report proceeds to tell the G.P. exactly what he should read, "at least one highbrow article per week," etc. It strays away from medicine to suggest the type of book he should read in his leisure hours. Some doctors will consider this latter an impertinence, others as a joke, but surely none will take it seriously. The solution of maintaining and raising the standard of general practice is simple, and has been reiterated *ad nauseam* in your columns. Basically, a higher capitation fee will allow more time to be spent on fewer patients, and the rest will follow. There is no need to send the trainee on expensive non-productive hospital courses, where he may be tempted to change his mind and swell the bursting ranks of the embryo specialists.

The modern tendency for more and more committees to lay down more and more rules for their fellow men is to be deplored. Throw away the controls and restore the freedom. Only in this way will the standard of recruitment to the profession be maintained and prevent the more individualistic members settling abroad to practise their great art.—I am, etc.,

London, S.E.1. ALLAN MATHESON.

Double Primary Carcinoma

SIR,—In relation to the correspondence on this subject, the following case seems to be worth recording.

In 1932 I removed the right breast of a woman by Halsted's operation for extensive cancer. She was then 52 and was the mother of nine children. Four years later she developed a cancer of the cervix. This was treated with radium by Mr. Ian Robertson at the same hospital, the Royal East Sussex. Both growths were proved by section to be cancerous. She had no recurrences, and is now a healthy woman in her 70th year.

The interest of the case lies not only in the double primary carcinoma, but in the fact that the patient was fortunate in recovering from both.—I am, etc.,

Hastings. HARRY GABB.

The Meaning of Observation

SIR,—Sir Henry Souttar's oration on "Observation" (May 27, p. 1219) taken in conjunction with Professor F. C. Bartlett's Oliver-Sharpey Lectures[1] on "The Measurement of Human Skill," lends support to the view that in the human subject the conditioned reflex, with all its subconscious ramification and reasonings, may be the highest state yet reached in the development of the mind. Easy access to the pool of knowledge, first built up and then reactivated by repeated observations, is essential to the clinician in the stress of modern practice, so that signs denoting emergency may rapidly and unmistakably be recognized.

To understand more fully the problem of how to develop and improve this faculty in doctors it must be recognized that while these subconscious processes reach a very high standard in some matters they can also stop short at a very low level. In each separate brain each separate subject has a limit beyond which further absorption cannot take place and beyond which observation cannot call forth any conditioned reflex.

An actual analysis taken from a medical student, and I believe typical of most, shows the limits of absorption for him: Latin and German, of third form standard; mathematics, short of the binomial theorem and logarithms; electricity, practically zero—the difference between watts, amperes, and ohms being completely uncomprehended; physics and organic and inorganic chemistry, of matriculation standard; other subjects, knowledge advancing satisfactorily with teaching. Above these limits true knowledge cannot be acquired, but memory for written words comes into play and examinations are passed. This conditioned reflex is on a much lower level, and merely facilitates a repetition of words. (Though essential to the musician or actor note or word perfection alone can never make a first-class artist.) It may be that the brain, subconsciously realizing its perversion, rapidly eliminates such memories from the student's mind. Certainly such "learning" is soon forgotten.

Bearing such data in mind, it is obviously waste of valuable time to insist on the re-examination of a student on grounds of insufficient knowledge of one or two subjects provided that in his others he has shown ability. His limited capacity for utilizing observations in those subjects stays in its former low state—word memory eventually allows him to deceive the examiner and to secure a pass. Fortunately this fact is becoming recognized at matriculation level, but it could with advantage be extended to the intermediate science stage. The student himself soon sizes up his own capabilities and, realizing his limitations

as regards electricity, physics, or chemistry, at once eliminates radiology, ophthalmology, or pathology from his final choice of vocation.

If somewhat disquieting conclusions may be drawn from this letter they are entirely due to viewing the problem from the wrong angle—that a broad education of a so-called high standard is necessary for success. If we start with the acknowledged fact that all successful general practitioners are very highly skilled clinicians, analyse the progress in obtaining their skill, and ruthlessly remove all hindrances found, and if we are willing to modify our cherished beliefs, then we shall be more aware of the meaning and importance of observation and will be able to put it to practical use.—I am, etc.,

Hove, Sussex. FRANK PORTAS.

REFERENCE

1 *British Medical Journal*, 1947, 1, 835 and 877.

The G.P. at the Crossroads

SIR,—At the last meeting of the Sydenham District Medical Society the Collings report was considered and a serious view was taken of its implications. In the end the following resolution was proposed and carried: "That any body appointed to investigate general practice should consist in the main of active G.P.s."—I am, etc.,

London, S.E.20. G. DE H. DAWSON, Hon. Secretary, Sydenham District Medical Society.

SIR,—Your correspondent Dr. A. Sanjana (May 20, p. 1201) maintains that in industrial practice time and unnecessary calls were as numerous under the "club" system as under the N.H.S. Before the appointed day the Birmingham Public Medical Service, which catered for the needs of hundreds of thousands of working-class people, imposed a fee of 3s. 6d. for a visit when the message was received after morning surgery hours and 5s. for a visit requested between 8 p.m. and 8 a.m. With the coming of the N.H.S. the number of late calls has increased enormously, and the great majority of these late calls could either have been put in in time or else allowed to stand over until next morning. Allied to this is the now prevalent practice of stopping the doctor on the road and requesting that he break into an already large list, thereby upsetting any effort he may make to plan his day. (This type of call is, in industrial practice, referred to as a doctor's "ice-cream trade.")

The imposition or reimposition of a small fee for late calls, to be waived at the doctor's discretion in really deserving cases, would appear to be both logical and justified. Not even the most idealistic Socialist quibbles (in public at any rate) at the principle of extra pay for overtime work. In case the managers of political parties might feel perturbed at its effect on voters, it is not out of place to state that on many occasions I have been offered recompense, either in cash or kind, after dealing with a late evening call. "We know it means extra work, Doctor, so perhaps you will accept this"—and "this" has varied from a pound note to a propelling pencil. The point is that most decent-hearted people would not resent a small fee, and the others would learn to put in their calls in time.—I am, etc.,

Birmingham, 14. W. M. E. ANDERSON.

Blood Loss at Operation

SIR,—The main reason for setting up a blood transfusion during or immediately prior to operation is to endeavour to maintain a constant volume of circulating blood, thus sparing the cardiovascular system from the necessity of adopting its natural defensive mechanisms. If one could gauge accurately the amount lost and the rate of loss the replacement would obviously be more successful. The estimation of this blood loss appears a difficult procedure in the theatre for obvious reasons, but, although a seemingly naïve approach to the problem, some idea may be obtained from a study of the used swabs laid out for counting in accordance with the results of the following rather crude experiments.

1. Two different types of swabs were taken, one of gauze 12 in. by 8 in. (30 by 20 cm.), and the other of butter muslin 12 in. by 12 in., folded *secundum artem*. These were then used to mop up known quantities of blood from a syringe. It was found that with butter muslin 16 ml. of blood saturated the swab completely; 10 ml. of blood just coloured the swab red throughout; with 7.5 ml. of blood white patches could always be found; 5 ml. of blood colours about half the swab; and 1 ml. gives the minimum of colour. With gauze 20 ml. of blood saturated the swab completely; 12 ml. coloured the swab completely; 10.5 ml. could only colour the swab red with diligent mopping; and with 5 ml. of blood many unstained areas were visible. Generally there seemed to be three types of dab: (1) fully soaked, equivalent to 10 or 12 ml.; (2) particoloured, equivalent to 5 or 7.5 ml.; (3) less than 5 ml.

2. Packs of turkish towelling 6 in. by 8 in. when dry would easily contain 100 ml. of blood, but when wrung out in saline would only take up to 50 ml., from which 45 ml. could be recovered by squeezing, and thus a discarded pack, although apparently well stained, only contains about 5 ml.

3. Using linen as towelling, it was found that 1 ml. of blood covered an area 3 in. (7.5 cm.) square.

Obviously these results cannot claim to be anything but approximate, since they depend on individual judgment and opinion, not to mention all the other variables which may occur, and better methods no doubt are possible. Nevertheless, if the general pattern of used swabs be considered the above method will give some idea of the blood loss and provide a pointer in deciding a little more accurately how many bottles of blood may be required to maintain the optimum volume of circulating blood.—I am, etc.,

Wrexham, Denbigh. JOHN MARCHANT.

"Disprin" Tablets

SIR,—In reply to the letter of the proprietors which recently appeared in the *Journal* (May 13, p. 1139), the pamphlet in the form of a brochure to which I drew attention was sent to me unsolicited with a bottle of tablets on January 14, 1949, together with a covering letter which includes the following sentence: "It is a preparation which rapidly dissolves in water to give a neutral solution of calcium aspirin." On January 18, 1949, further samples and similar literature were again sent to me, and since then further similar brochures in all of which my name appears as a reference. This brochure is of interest because it is stated therein (p. 6): ". . . when placed in water, a *substantially* neutral solution of calcium acetyl-salicylate results from the interaction" (italics mine).

In the even smaller booklet which accompanies the bottle of tablets as usually sold to the public direct it is stated (p. 4) that ". . . a tablet dropped into water produces a neutralized (non-acid) solution of calcium aspirin." Further on (line 16) "disprin" is described as "being completely soluble," and on p. 5 it is again stated, "Being entirely neutral (non-acid) and soluble disprin is especially suitable . . ."

On the question of stability I would draw attention to the advertisement which appeared in the *Proceedings of the Royal Society of Medicine* (February, 1950, p. xiv) wherein it is stated, "Disprin rapidly dissolves in water to yield a solution of calcium aspirin, neutral, stable, palatable, and pure." My relevant analytical data do not confirm these claims. It has now been admitted that the *p*H of the solution is in the region of 4.5 (each tablet contains 3 gr. approximately of insoluble starch) and I am content to leave it to the judgment of others whether the phraseology "substantially neutral" employed by the proprietors of disprin tablets should not read "substantially acid." Personally I am unaware of having stated at any time that "the *p*H . . . 4.7 . . . represents neutral calcium aspirin."—I am, etc.,

London, N.W.4. M. COPLANS.

Chlorosis

SIR,—Dr. M. D. Warren (May 20, p. 1204) reminds us of the references to chlorosis in the medical literature of the past two hundred years, pointing out that the clinical picture of this condition seems to have changed somewhat during this period. From the literature he cites it would appear that amenorrhoea or dysmenorrhoea was uncommon at the beginning of the nineteenth century, but that by the end of that century Osler at least had come to recognize the fact that "menstrual disturbances are very common."

In the light of this and the description of the condition as given by Dr. R. K. Steen (April 20, p. 962) it may be of interest to note the description given by Hippocrates in his book on the diseases of virgins, quoted by Johann Lange in his book

Medicinalium epistolarum miscellanea published in Basle in 1554. Lange, quoting, writes:

"Virgins . . . to whom the time of marriage comes, and are now mature, are afflicted with imaginary terrors of spectres, especially when the menses appear, for before this they are not at all badly affected, afterwards indeed the blood in the small spaces of the womb, as it were escaping, drips and falls, since the obstructed mouths were the places of egress, and the blood abundant from the foods and the growth of the body, collected there, is present in large quantity and whence it flows distending the opening of the veins, the heart beyond its power moves up to the septum transversum and diaphragm, the heart itself does not hold out and becomes torpid, then from this torpidity the patient becomes foolish and delirious. It is certainly no wonder since the liver is not cleansed of the filthy blood of the menses, and by it the veins of the diaphragm are stopped up, the viscera of the abdomen swell, and the diaphragm is contracted (as in hydrops), then a difficulty in breathing appears. . . ."[1]

Lange prefaces these observations with some comments and observations of his own in the chapter entitled "De morbo virgineo":

"Nor has this disease a proper name. . . . But this disease frequently attacks virgins, when now mature they pass from youth to virility. For at this time, by nature, the menstrual blood flows from the liver to the small spaces and veins of the womb: which when from the narrow mouths, which are not yet distended also obstructed by thick and crude humors, and finally from the thickness of the blood, cannot escape. . . ."[1]

The treatment, he says, is "venesection if nothing hinders."

As the above comments are not my own but those of the fathers of medicine, I took courage and feel justified in making these additional contributions, which seem, to me at least, to show that in so far as menstrual changes are concerned chlorosis has not materially changed since it was described in the fifth century B.C.—I am, etc.,

London, W.1. D. H. TRAPNELL.

REFERENCE

[1] Major, R. H., *Classic Descriptions of Disease*, 1945, Springfield, p. 488.

Typhoid Fever Treated with Chloramphenicol

SIR,—A number of reports have appeared in English literature about the effect of chloramphenicol in typhoid fever. It seems worth putting on record the successful treatment with this antibiotic of a child suffering from this disease.

The patient was a girl aged 5½ years. One month earlier the child was nearly drowned in the River Lea in London. After recovery she was well until five days before admission, when she became ill and developed high fever. Diarrhoea was not a prominent feature. She was put on sulphadiazine, but did not respond and was therefore admitted to hospital on the sixth day of her illness.

On admission the girl's temperature was 105° F. (40.6° C.), the pulse was 150, and respirations 40. The temperature fell to normal the next morning but rose later in the day to 103° F. (39.4° C.). The pulse fell to 120–130. The tongue was dry and coated. She was in no pain, no rash was observed, and no abnormal signs were present in the chest or central nervous system. There was no neck rigidity, and Kernig's sign was negative. The abdomen was soft, and there was no tenderness. The spleen was not palpable. The child passed one stool only during the first three days in hospital: this was somewhat relaxed but otherwise normal, and no blood was present. The temperature fluctuated between 102° and 103° F. (38.9° and 39.4° C.), and the pulse was 110–120. On the third day after admission the child had an epistaxis while a lumbar puncture was being done.

The blood findings were: R.B.C.s 4,790,000, W.B.C.s 10,300 (polymorphs 68%). The urine and C.S.F. were normal.

Three days after admission the child began to pass more frequent stools, which were loose in character and in number about two to three daily. The abdomen had become a little distended and there was a slight degree of general tenderness. The tongue was dry and covered with a brownish fur. The spleen could not be felt, but it became palpable on the eleventh day of the illness. In order to establish a diagnosis the serum agglutination reactions were tested, and blood was taken for culture. A positive agglutination to the H agglutinin of *Salmonella typhi* was obtained. The blood culture gave a growth of *S. typhi*, which was also grown from the stool but not from the urine. On the seventh day after admission (thirteenth day of illness) there was an agglutination titre of 1 in 500 to the H agglutinin of *S. typhi* and a titre of 1 in 250 to the O agglutinin. The *S. typhimurium* was also agglutinated to a titre of 1 in 125.

The diagnosis was not finally established until the eighth day of the illness, and on the morning of the ninth day administration of chloramphenicol was commenced. The dosage was six capsules (1.5 g.) immediately, followed by two capsules (0.5 g.) twice daily for eight days and thereafter one capsule (0.25 g.) twice daily for fifteen days. The total dosage of the drug was 17 g. There was no difficulty in getting the child to swallow the capsules, which were well tolerated and did not provoke nausea.

On the evening of the tenth day the temperature was 102° F. (38.9° C.) and it rose to this figure also the next evening. On the twelfth day the temperature began to fall and reached normal on the morning of the fourteenth day. The tongue became cleaner and the abdomen less distended and tender. The stools underwent little change: they were loose and about two to three a day in number. After the fifteenth day the stools were much less frequent and gradually became normal. The general condition of the child improved rapidly and her appetite returned. A negative stool culture was obtained one week after chloromycetin was first given.

The temperature remained normal until the twenty-third day of the illness, when it rose to 100° F. (37.8° C.). The stools were normal and there was no change in the condition of the child. The slight pyrexia continued, however, and two days after its onset a swelling appeared on the right side of the face. The child complained of toothache at the site of a carious molar. After removal of the carious tooth the swelling subsided and the pyrexia settled. No further complications occurred. The child was seen one month after discharge. She had remained very well and was considered fit to return to school.

There seems no doubt that in this case the sudden improvement and rapid recovery was the result of chloramphenicol therapy.—I am, etc.,

London, W.1. GEORGE H. NEWNS.

Student Health and Welfare

SIR,—As physician in charge of students' health at Queen's University, Belfast, I was very interested to read the annotation on student health and welfare (April 29, p. 999). It was pointed out there, among other comments, that the majority of such schemes were voluntary and therefore liable to be misleading in their statistical implications. At Queen's University, Belfast, compulsory examination, Mantoux test, and *x*-ray examination of the chest on entry were instituted in 1944, and this was carried a step further in 1949, when all students at the University were required to have an annual *x*-ray examination of the chest.

I know that the question of making students' health schemes compulsory has long been a thorny topic of discussion, and apart, therefore, from our statistical results I thought the reaction of the students here might also prove of interest and value to other universities who are hesitant about instituting such a step. Our experience has proved that if undertaken in the proper manner no resentment need be experienced from the student population, and it would be eventually accepted as a necessary part of their curriculum. Increasing numbers of students coming up to the university have had chest radiographs done in their secondary schools and not only accept the fact that this practice will be continued but even expect it.

I feel quite sure that where the scheme is voluntary the majority of those who default do so from sheer negligence rather than resentment, while a few already known victims to tuberculosis, however quiescent or healed, fear that they may not be allowed to continue their university careers should their condition be revealed. There were no defaulters either among the first-year students or the whole student body for the first annual *x*-ray examination of the chest in 1949. As regards the latter, the most important factor was that this measure was strongly advocated by the students themselves through the Student Representative Council, and with their co-operation no difficulty was experienced in carrying out the survey. Also the mass miniature radiography unit was brought to the university for a month, and as far as was practicable with such large numbers students were encouraged to make their own appointments, and every care was taken to avoid interference with their academic studies. The staff of the university were invited to participate, and their response was, I am sure, an excellent example to the students.

In all 2,427 students (1,914 males and 513 females) were radiographed, and among these 7 active (5 male and 2 female) and 34 inactive (28 male and 6 female) cases of pulmonary

tuberculosis were revealed. The age and sex distribution, which will be of interest to other workers in this field, are shown in the accompanying table.

Age	Males			Females		
	No. Radiographed	Pulmonary Tuberculosis		No. Radiographed	Pulmonary Tuberculosis	
		Active	Inactive		Active	Inactive
18– ..	371	1	4	126	1	1
19– ..	264	—	—	102	—	1
20– ..	234	1	3	76	1	1
21– ..	204	—	3	58	—	—
22– ..	175	—	1	37	—	—
23– ..	171	—	4	51	—	—
24– ..	115	2	1	22	—	—
25– ..	268	1	8	24	—	1
30+ ..	112	—	4	17	—	2
Total	1,914	5	28	513	2	6

Of the seven active cases discovered, none of which were previously known, two are now back at the university (three months later) with the condition arrested, while the other five are making satisfactory progress. The 34 inactive cases, of which 21 were already known, are under regular surveillance and have been advised about their future mode of life. Every care has been taken to avoid introducing any psychogenic factor, and I know of no case where this has occurred.

One other item in our scheme which I do not think is universal was the institution of B.C.G. vaccination on a voluntary basis to all Mantoux-negative reactors. This was commenced in July, 1949, and so far approximately 100 cases have been completed—with 100% conversion and no reactions. These 100 cases represent approximately 60% of the negative reactors offered B.C.G.—and here again inquiries have shown that the majority of the remaining 40% who have not volunteered have, in the casual way of students, simply ignored or forgotten all about it.—I am, etc.,

Belfast. W. JOHNSTON.

Student Congress: Disclaimer

SIR,—It has come to our notice that a student political body has recently been appealing to doctors and other interested persons for funds to send medical students to the World Student Congress at Prague in August.

On behalf of the British Medical Students Association I would like to call attention to the fact that this political body has nothing whatsoever to do with our association. The B.M.S.A. will send one representative to Prague on behalf of British medical students, and we are not issuing an appeal for funds.—I am, etc.,

P. L. C. DIGGORY,
London, W.C.1. President, British Medical Students Association.

Urinary Infection Treated with Chloramphenicol

SIR,—The following case, demonstrating the efficacy of chloramphenicol in a *Ps. pyocyanea* urinary infection, should prove of interest.

The patient, a married woman aged 56, was admitted to the Wilson Hospital on March 29, 1950, for investigation of a dull ache of six months' standing; she indicated the anterior part of the left costal margin, the left flank, and both groins as the seat of the pain. Later investigation suggested that the latter was psychogenic and unrelated to the subsequent history.

On April 12 she complained of pain shooting down the left leg, and two days later *Ps. pyocyanea* was grown on culture from the urine. A further culture on April 20 yielded the same result. A previous intravenous pyelogram had shown the right upper calyx to be separated from the middle calyx, possibly by a cyst, and multiple kinking of the upper ends of both ureters. In view of the possibility of obstruction and the desirability of retaining streptomycin for use in conjunction with surgical measures should these later seem necessary, it was felt undesirable to use streptomycin. The risk of development of resistance to this agent, which the absence of an unimpeded urinary flow rendered probable, seemed too great.

However, on April 23 she had several sharp bouts of pain in the left flank, together with a rigor. She was found to be tender in the left costovertebral angle. On April 26 a catheter specimen of urine still revealed *Ps. pyocyanea* on culture. Chloramphenicol was given, 1 g. eight-hourly for two days, and then 0.25 g. eight-hourly for a further week. Twenty-four hours after starting the drug the urine had become sterile, and remained so. A week after discontinuing the chloromycetin the urine was still sterile upon culture.

—I am, etc.,

Mitcham, Surrey. L. C. HURST.

Spinal Analgesia for Caesarean Section

SIR,—Mr. Stafford Matthews's recent letter (May 27, p. 1269) makes it very difficult for those of us now working under infinitely better conditions to offer any real criticism. Those who have already appeared to give offence can only offer apology, knowing it will be graciously accepted, and those of us whose interest in anaesthesia for caesarean section prompts us still to write could only make suggestions the implications of which Dr. A. H. C. Walker and Mr. Matthews are perfectly well aware already.

Certainly the prospect of Dr. Walker now reverting to the use of open ether following the catastrophes under spinal analgesia tempts me to hope, so far as it may interest the senior anaesthetic registrars now "waiting," that heed may be taken of Mr. Philip Mitchiner's advice (*Supplement*, May 13, p. 219) in his guise of a modern Greeley "to go East young man." The conditions under which they have to work and the tremendous task of attempting to attain to the high standards they knew previously also makes one feel that much more ought to arise out of the remarks of the consulting physician to the Sudan Government (*Supplement*, May 27, p. 243).

Having since the war had the immense advantage of the assistance of Dr. T. C. Gray and his team in the Liverpool area, who have skilfully administered anaesthesia for caesarean section using the curare–"kemithal"–cyclopropane sequence, I have now almost abandoned the use of spinal analgesia, and since I also make exclusive use of the Pfannensteil-type of incision for the lower-segment operation it can offer me nothing from any aspect which the curare sequence cannot. Whatever type of anaesthetic agent is used, no one I think could possibly disagree with the view which Pugh Thomas and I have previously expressed in discussing the causes of fatality from anaesthesia that only by the combined and persistent exertions of surgeon and anaesthetist working together as a team can this tragedy be indefinitely delayed.[1] No one will agree with me more readily than Dr. Walker and Mr. Matthews, so far as their conditions of work now obtain, that their unfortunate experience may very well be repeated unless there be some change in official policy towards the provision of adequate personnel and supplies.—I am, etc.,

Liverpool. H. VINCENT CORBETT.

REFERENCE

[1] *J. Obstet. Gynaec. Brit. Emp.*, 1949, **56**, 632.

Corticotrophin in Rheumatoid Arthritis

SIR,—The article by Professor H. N. Green on a suggested mode of action of corticotrophin in rheumatoid arthritis and the allergic state (May 20, p. 1165) is most arresting, for not only does it give us an insight into the pathogenesis of rheumatoid arthritis but also into that of malignant disease. We are so accustomed to state that such and such a patient is allergic, but do we know what allergy connotes? One thing we know about it for certain—it is always accompanied by an eosinophilia.

Unfortunately the part played by the eosinophil in the human economy is not exactly known, but I think it can be surmised that it is a repair cell which can adapt itself to surrounding conditions and ultimately assume the function and role of the cell it has been called upon to replace. Is it not the eosinophil cells of the anterior pituitary which are concerned with growth? Eosinophils can be found in tumours, the base of peptic ulcers, and in Hodgkin's disease. In the inflammation of any tissue, while the neutrophils are active, the eosinophil is repelled, but when the acute stage is over it is rushed to the spot—a good omen, as it indicates the termination of the toxic stage and the commencement of the stage of repair. As one writer puts it:

"We find it hard to believe that the allergic reaction can have been evolved in the course of nature other than for the protection or the benefit of the individual. Allergy is a virtue which, like any other virtue, becomes a vice when pushed to excess."[1] And so in excessively allergic individuals where there is a hypereosinophilia the supply is greater than the demand; the invasion indeed has been on too big a scale, with the result that the eosinophils form a colony of their own—in other words a new growth. Excessive allergy releases the spring which keeps these cells in check. One can understand why secondaries appear in malignant disease when we realize that the eosinophils are drained off by the lymphatics.

What observations, experimental and clinical, can be advanced to substantiate this theory? Professor Green's article makes it clear that by arresting the production of eosinophils skin mitosis ceases entirely or is much depressed for at least seven hours, and granulation tissue formation fails and chondro-osteogenesis is inhibited. "Even the proliferation of malignant cells is, in some cases, depressed, for there are now reports that the treatment induces temporary depression in acute leukaemia. It would therefore not be surprising if a striking general as well as local improvement proves to be an indication that a hypersensitive state exists." In Blair Bell's lead treatment of cancer, where undoubtedly there was regression in some of the growths, there can be only one explanation of the therapeutic action of this heavy metal—it induced an eosinopenia: so with gold in rheumatoid arthritis. Gold, too, has been used with varying degrees of success in pulmonary tuberculosis, where Dr. Wingfield has made out a strong case for excessive allergic reactions being responsible for the sudden appearance of secondary deposits in a lung or some portion of it previously unaffected.[1]

For some years I have thought of a possible connexion between allergy and malignant disease, and so looked up the records of a series of 47 cases of cancer occurring in my practice. In all save one there was an allergic family history. I have seen, too, rheumatoid arthritis and cancer follow asthma, which then disappeared. It is just possible that these three diseases—asthma, rheumatoid arthritis, and cancer—are prone to develop in the allergic, which means that they should all be treated by agents which lessen the production of eosinophils.

Professor Green's article brings us nearer to the solution of the cancer problem than we have ever been, and I very much look forward to the publication of the results of his further investigations.—I am, etc.,

Upholland, Lancs. J. THOMSON SHIRLAW.

REFERENCE

[1] Wingfield, R. C., *Brit. J. Tuberc.*, 1934, **28**, 155.

Dosage of Streptomycin

SIR,—I have recently been using the following routine dosage in the treatment of pulmonary tuberculosis—1 g. of streptomycin twice a week, and 12 g. of P.A.S. daily (given as 3 g. four times daily). I have so far only given this dosage to 12 cases (not all completed), but I have been pleased with the results as judged by the effects on fever, weight, symptoms, and (usually) radiographic shadows and B.S.R. I believe the method has certain advantages which may be listed as follows: (1) convenience, especially in domiciliary treatment; (2) reduced risk of toxic effects from the streptomycin (I have not yet encountered such effects with this dosage); (3) no tendency to develop streptomycin "resistance" has yet been discovered, though most of the cases have been "advanced," with large cavities and massive *x*-ray shadows.

It may be proved eventually that concurrent administration of P.A.S. tends to prevent the production of resistant strains whatever the type of case. I do not think we can assume this yet, and I think that the use of a low-dosage scheme may also contribute to this desirable result. The two M.R.C. reports on streptomycin give some support for this contention. There is evidence that in comparable types of disease it is the total amount of streptomycin given which is the chief factor in determining if resistance will develop. Hence a low dosage may allow a much longer period of treatment without any development of resistance. I hope that others will try this dosage, and if it should be found that it is both effective and free from harmful effects the indications for chemotherapy might be widened. Different dosages might, of course, be best for different types of case—for instance, higher dosage might be preferable for an acute spread following thoracoplasty.—I am, etc.,

Bradford-on-Avon, Wilts. R. L. OSMASTON.

Presenting Signs of Cholecystitis

SIR,—An inflamed gall-bladder is of course notorious for presenting itself in many guises. I think, however, the three following cases are sufficiently unusual to merit recording. In these cases inflammation of the gall-bladder presented as indicated.

1. *Haematemesis.*—Patient was a woman in the early forties who gave a history of some gastric upset of short duration, with epigastric pain, and who was brought into hospital with a rather copious haematemesis. This subsided under treatment but was repeated two or three times, and the physician in charge asked me to undertake the case surgically.

At operation the stomach was found to be normal, but the gall-bladder was chronically inflamed, contracted round some stones, and strongly adherent to all surrounding organs. On dissecting away these adhesions it was found that the portal vein was stuck to the middle of the gall-bladder and was pulled quite an inch out of its normal position, kinked, and therefore obstructed. With a great deal of rather nervous dissection the portal vein was dissected clear of the gall-bladder, which was removed. The patient had no more haematemesis. The diagnosis was made of portal obstruction causing oesophageal varices. The patient died in the same hospital about two years later from a completely unrelated condition, having had no further bleeding. At necropsy the diagnosis of old oesophageal varices was confirmed.

2. *Hour-glass Stomach.*—This patient, another middle-aged woman, had had a long "gastric" history and *x*-ray examination revealed an hour-glass stomach with a marked constriction. At operation a large mass of the omentum was found passing upwards across the middle of the stomach to be attached to a chronically inflamed gall-bladder. The stomach was in no way adherent to this omentum. On dividing the band, which caused an almost complete obstruction across the middle of the stomach, the latter organ regained its normal shape almost immediately. This was obviously due to the fact that the actual portion of stomach contracted must have been continually varying with the patient's position and the stage of gastric digestion.

3. *Large-bowel Obstruction.*—This patient was a man of about 45 who came up with a history of an absolute constipation for three days, with no flatus passed and with abdominal pain and distension. The abdomen was distended and tympanitic over the caecum and up the ascending colon, the tympanites ceasing at the midline. The descending colon was collapsed. *X*-ray examination revealed a greatly distended caecum, ascending colon and lateral half of the transverse colon, with much gas and fluid, and a collapsed descending colon. The only anomalous feature was a temperature in the neighbourhood of 100.6° F. (38.1° C.). At operation a gall-bladder was found with the walls grossly oedematous, with patches of necrosis, and with a completely necrotic mucous membrane. Surrounding the gall-bladder was a space filled with blood-stained fluid and, forming the lower wall of this space, was the great omentum, which was curled upwards and was completely obstructing the transverse colon about its midline. The caecum and colon up to this point were grossly distended. The omentum was freed and the gall-bladder removed, and the patient is making an uninterrupted recovery.—I am, etc.,

London, E.C.2. A. J. HOBSON.

The Opaque Catheter

SIR,—From time to time during retrograde pyelography a ureteric catheter is found to be non-opaque. This causes difficulty and sometimes delay to surgeon and radiologist alike. I understand that in the past opaque catheters had a slightly shorter life and were a little more brittle than the non-opaque

variety. If this difficulty has been overcome why should not all ureteric catheters be opaque to radiation? If not, would it be too much to ask the manufacturers to agree on standard distinctive colours for each type?

In the case of existing catheters in use a distinction could readily be made by fixing them at equal distances across an *x*-ray film with adhesive plaster. An opaque letter could be put at one end of the film. After exposure the non-opaque catheter would reveal itself by the presence of a gap.—I am, etc.,

Bournemouth. G. L. BUCKLEY.

Intestinal Obstruction Due to Food

SIR,—Mr. Neil Ward-McQuaid in his instructive article (May 13, p. 1106) said that he has been unable to trace any case report in which meat was the obstructing agent, apart from some cases in South America. I am able to record the following case in which a bolus of undigested meat caused fatal obstruction.

An edentulous woman, aged 53, was admitted to King Edward VII Hospital, Windsor, on November 24, 1938. She complained of an acute colicky epigastric pain of 30 hours' duration, with constipation and repeated vomiting. Abdominal distension was noticed on the day of admission, and a little flatus was passed with an enema given before admission, but no faeces. She had previously been in good health and had had no serious illness and no abdominal operations.

On examination her temperature was 98° F. (36.6° C.) and pulse 108. Her tongue was dry and furred, her breath offensive, and she was pale, anxious, and dehydrated. The abdomen was distended and tympanitic, with tenderness mainly in the midline below the umbilicus. Peristaltic sounds were increased on auscultation, but no visible peristalsis was present. There was no external hernia, and rectal examination revealed an empty rectum with no pelvic tenderness.

A diagnosis of acute small-intestine obstruction, probably due to a band, was made, an intravenous saline drip set up, and the stomach aspirated with a Ryle's tube. At operation coils of distended small intestine were found with some early peritonitis and turbid free fluid. A firm oval foreign body was found impacted in the lower ileum some 40 cm. above the ileocaecal valve. The caecum and ileum below the point of impaction were empty, and there was no evident perforation. The foreign body could not be pushed on or broken up by finger pressure, and accordingly the ileum was opened between clamps, the foreign body removed, and the incision closed transversely in two layers. The foreign body measured 5 by 2 by 1.5 cm. and appeared to consist of undigested meat. This was confirmed by microscopical examination, which showed that the foreign body mainly consisted of striated muscle fibres and faecal material. The patient developed paralytic ileus and died from acute peripheral circulatory failure 36 hours after operation.

On questioning the relatives it was discovered that this patient had had a meal of steak-and-kidney pie the day before the onset of symptoms, and it appeared that she was in the habit of bolting her food, due no doubt to her lack of teeth.—I am, etc.,

Windsor. R. VAUGHAN PAYNE.

Congenital Heart Disease and Dissecting Aneurysm

SIR,—The note on congenital heart disease by Dr. Marjorie Crumpton (June 3, p. 1303) is unfortunately misleading. This was published without consultation with any of us. The information obtained by Dr. Crumpton, as an observer at the necropsy and from the provisional report sent to the ward where she was house doctor, is accurate only so far as the investigation had gone at the time. Similarly the diagram has apparently been based on a speculative drawing which was made then, before the heart had been opened fully. The facts discovered since Dr. Crumpton left the Infirmary show that the conditions in the heart are rather different from those described by her.

We regret that Dr. Crumpton had believed that the pathological investigation was completed and hope that your readers will be prepared to await a more detailed description of the condition. This has been under study for some months and will be published by one of us (H. G. M.)—We are, etc.,

J. GORDON CLARK.
A. C. LENDRUM.
H. G. MORGAN.

Royal Infirmary, Dundee.

SIR,—Since the publication of my medical memorandum (June 3, p. 1303) on congenital heart disease and dissecting aneurysm of the pulmonary artery it has come to my notice that further pathological study of the heart mentioned is being undertaken, and it seems likely that the appearances first noted were deceptive and the ultimate classification will differ from that suggested in my article. I apologize for misleading readers, but I had no reason to believe that investigation of the specimen was incomplete.

At all events, the prime object of my publishing the case was not to discuss the pathology of congenital hearts—I leave that to the experts—but to indicate two points of interest: (1) the age to which the patient lived with relatively little disability; and (2) the most unusual cause of death. The presence of gross developmental abnormality was obvious, and I shall be extremely interested to learn the ultimate pathological classification of the condition.—I am, etc.,

East Newport, Fife. MARJORIE CRUMPTON.

Streptomycin and Reiter's Syndrome

SIR,—The interest of this case lies in the fact that I believe it to have been the first case of Reiter's syndrome treated with streptomycin and "sulphamezathine."

The patient, an intelligent, well-developed male aged 36, had his first attack of polyarthritis, non-specific urethritis, and conjunctivitis in the Army in August, 1945. He then remained symptom-free until his relapse in October, 1949. The history of the original attack was as follows (extracts from Army case-papers).

In August, 1945, non-specific urethritis was diagnosed and treated with 25 g. of sulphathiazole. Two weeks later the patient had hypogastric pain after micturition, and 24 hours afterwards pain in the right knee and back together with bilateral conjunctivitis. Mild silver protein drops cleared the eyes, but despite 144,000 units of penicillin intramuscularly the patient became feverish, and the knees, ankles, and toe-joints swelled and hurt. During the next three days he received a further 180,000 units of penicillin and a salicylate mixture. There was then slight improvement, but ten days later he was still febrile, his left eye again became inflamed, and the large joints of both arms were affected. The patient says that at this stage he was given great relief by intravenous injections of N.A.B., but there is no record of this in his Army medical records.

The condition gradually cleared, the knee-joints being last to recover, and four months later he resumed duty.

The history of his recent attack was as follows. In October, 1949, the patient noticed a urethral discharge and a heaviness in the hypogastrium after micturition. About four days later there was a bilateral conjunctivitis and pain around the knee- and hip-joints.

On examination, the urethral discharge showed no Gram-negative diplococci, and there was an abacterial pyuria. There was a little fluid in both knee-joints, with marked peri-articular swelling. The blood examination showed: Hb, 87%; polymorphs, 80%; eosinophils, 1.0%; colour index, 0.89; B.S.R., 47. The Kahn and Wassermann reactions were negative, and also the gonococcal complement-fixation test. Four shallow ulcers now appeared on the glans penis, and there was extensive shedding of the horny layers of the skin of the soles of both feet. The patient was given "albucid" eye-drops, and obtained prompt relief. "Benadryl" (50 mg. four-hourly) was also given to deal with any allergic factor. Benadryl, probably by a central sedative action, relieved the hypogastric discomfort.

The painful swellings of the joints persisted, all the limb joints and the temporo-maxillary joints being involved in turn and for about 36–72 hours at any one time. More than one joint was usually affected simultaneously, and pain was most severe and persistent in the left wrist, right shoulder, and in both knees. During the second week in bed a fever of 99–101° F. (37.2–38.3° C.) appeared, and the urethral discharge dried up. General malaise now increased. Intravenous N.A.B. (0.3 g.) and salicylates pushed to the point of intoxication were ineffective. The blood examination now showed: Hb, 67%; B.S.R., 29. The Wassermann reaction was negative, and the result of the Kahn test was doubtful. A repeat test by the same laboratory was also doubtful. A further test, done by two different laboratories, both showed Kahn and Laughlen tests to be definitely negative. The gonococcal complement-fixation test was also negative.

Sulphamezathine tablets (1 g.) were now given four-hourly, and in thirty-six hours the temperature was normal—the first time for two weeks. After 48 hours there was again fever of 100° F. (37.8° C.), and 0.5 g. of streptomycin was injected intramuscularly six-hourly. For the next five days there was only fever at night (99–100° F.), and the B.S.R. was now raised to 43. Serum agglutination against *Shigella flexneri V* was positive at a dilution of 1 in 500. Other strains gave negative results. There was no history of

dysentery while the patient had served in Northern Europe, and no inoculations had been given which might have produced this rise in titre. By the time the patient had been given 30 g. of sulphamezathine and 10 g. of streptomycin his temperature had been normal for three days, and he felt much better. The B.S.R. was now 41, and Hb 83%. All limb joints showed radiological signs of early osteoarthritis.

Reiter's syndrome was regarded by Paronen,[1] in his review of 344 cases, as a self-limiting disease of 2–5 months' duration. Paronen decided that none of his methods of treatment, which included neoarsphenamine, sulphonamides, and fever therapy, produced a "prompt and general improvement." Intravenous arsenicals were used effectively by Baines[2] and by Khoury.[3] They were of no benefit in the present case. Penicillin and sulphathiazole were ineffective in cases studied by Morrison and Thomson[4] and by Baines, while Young and MacEwan[5] reported the sulphonamides as being useless in this disease.

The present case presented a swift fall in temperature after sulphamezathine, but this improvement appeared transient. The addition of streptomycin resulted in a stepping-down of the flickering temperature, which was steadily normal after 5 g. of streptomycin had been given. The ophthalmic, skin, and urethral manifestations had disappeared by the time sulphamezathine and streptomycin therapy commenced. Improvement in the general condition and in the arthritis was then accelerated, and no further joints became involved.

In this case of Reiter's syndrome, sulphamezathine and streptomycin were undoubtedly of benefit. There was no improvement in the B.S.R. to correspond with the lessening of pain and increased sense of well-being in the now afebrile patient. Dysentery has always been suspected to be an aetiological factor in Reiter's syndrome. Although there was no history of infection, the rise in serum agglutination against *Shigella flexneri V* in this case is of interest.

I am grateful to Dr. L. Davidson for his advice and permission to publish this case.

—I am, etc.,

Ilkley, Yorks. O. B. APPLEYARD.

REFERENCES

1 *Acta med. scand.*, 1948, Suppl. 212.
2 *British Medical Journal*, 1947, 2, 605.
3 *J. Urol.*, 1947, 58, 268.
4 *Lancet*, 1948, 1, 636.
5 *J. Amer. med. Ass.*, 1947, 134, 1456.

Mass Vaccination

SIR,—Allow me to endorse Mr. A. W. Fowler's contention (May 27, p. 1272) that in this country mass vaccination of the general population is not necessary for the effective control of outbreaks of smallpox, and that this measure should be reserved until such time, if ever, as the disease gets really out of hand. We have repeatedly seen mass vaccination resorted to in recent years where a limited outbreak has occurred—e.g., the outbreak in Glasgow last April, the outbreak in the same city in 1942,[1] and the outbreak in Edinburgh also in 1942.[2] Hundreds of thousands of persons were vaccinated, largely as the result of panic which the action of the authorities encouraged rather more than tended to allay, and in each of these examples the event showed that the outbreak was virtually all over before the vaccination campaign was even begun. The whole history of major smallpox in this country (I am not speaking of minor smallpox) since modern methods of dealing with it have been understood and efficiently carried out shows conclusively that such methods are adequate for the control of the disease without recourse to mass vaccination of the general population.

I believe I am right in saying that the two last occasions when major smallpox in this country really got out of control were at Gloucester in 1895–6 and at Dewsbury in 1904. That was before it was realized that the control of a disease like smallpox was a national, or at least a county, responsibility rather than a purely local matter to be dealt with unaided by each individual district, however small its resources for coping with a serious emergency. Gloucester had a population of 40,000, and the Dewsbury Union of only 27,000. Both places were served by a part-time M.O.H. in general practice, their sanitary staffs were necessarily small, and their hospital accommodation totally inadequate. In both cases we have a good example of how not to deal with smallpox. Any serious attempt to control the disease quickly broke down. The pitiable little hospitals quickly became grossly overcrowded and worse than useless, and a majority of the cases occurring had to be left to look after themselves at home—in some cases persons suffering from smallpox having to share a bed with healthy persons. In both places there was a strong prejudice against vaccination, and a large proportion of the child population was unprotected by vaccination. As a result the case mortality was necessarily high. But a large proportion of the adult population was partially protected, and this led to the occurrence of slight unrecognized cases which largely helped to spread the disease.

A study of the true story of these two outbreaks, for which at the time the neglect of infant vaccination was given the full blame, makes it clear that had modern methods of prevention been applied, as they would be applied to-day, both outbreaks would, almost certainly, quickly have been cut short. Fortunately, the lessons taught by Gloucester and Dewsbury have now been learnt, with the result that no similar instance of major smallpox getting out of control has since occurred.—I am, etc.,

Leicester. C. KILLICK MILLARD.

REFERENCES

1 *British Medical Journal*, 1943, 1, 288.
2 Ibid., 1945, 1, 304.

Co-ordination of Medical Services

SIR,—Should not the training of the G.P. be related directly to the future of the G.P.? Whatever else has been settled by the N.H.S. Act, surely the divorce of the G.P. from hospital work under the regional hospital board organization is certain. Would it not be wiser to recognize the fact and utilize hospitals for their teaching facilities in their relation to domiciliary work, which is quite certainly and essentially the G.P.'s province?

There is a side to this domiciliary work which was not apparently considered by the Cohen Committee—namely, the relationship of the G.P. to the local-health-authority service. The Act has shown that this is becoming closer than ever it was, since the nursing, midwifery, and home-help services are essentially adjuncts to the G.P. service, and should be part of one organization under the local executive council rather than the local county or county borough council.

Surely if a fusion of these services were made it would be possible to organize some health centres in association with some of the present clinics, and, since the local councils have been so decimated by losing their transport, gas, and electricity undertakings, there could be little reason for their retaining the crumbling edifice of their present priority dental and medical services. The lack of hospital nursing staff means an increasing need for domiciliary treatment of the sick. Has not the time arrived to review the domiciliary services to enable them to widen their scope by linking up the health-authority services inside the local executive council's organization?—I am, etc.,

London, W.5. W. G. BOOTH.

Epilepsy treated with Phenytoin Sodium and Phenobarbitone

SIR,—During the last three years considerable attention has been given to the treatment of epilepsy at the Midland Nerve Hospital, Birmingham. Special effort was directed to reduce (1) grand mal attacks, (2) petit mal attacks, and (3) epileptic equivalents or psychic epilepses. During the period under review over 200 patients, including males and females varying in age from 10 to 53 years, who had previously been treated with 1 gr. (65 mg.) of phenobarbitone t.d.s. were given combinations of phenytoin sodium with either phenobarbitone or phenobarbitone sodium. Phenobarbitone exerts its control of epileptic seizures by a depressant effect on the motor cortex. Phenytoin has only a weak hypnotic effect and its main action is anticonvulsant.

With the combination of phenobarbitone and phenytoin sodium, results were obtained very similar to those of Blair[1] and of Robinson and Osgood.[2] The combination of the two drugs gave results 16% to 20% better than either drug alone. It was found that phenytoin sodium combined with phenobarbitone sodium (which is the soluble salt) gave much better results. Of

the 200 cases treated thus, 50% showed entire cessation of seizures, both grand mal and petit mal, and 80% of these also showed entire cessation of epileptic equivalents. Another 45% of those treated showed marked reduction in the seizures and epileptic equivalents. Only 5% showed no marked change.

It was further found that to get the best results the phenobarbitone sodium and phenytoin sodium need to be given in the one tablet. The optimum dosage was found to be ¼ gr. (50 mg.) of phenobarbitone sodium and 1½ gr. (0.1 g.) of phenytoin sodium. Apart from that, the ease of administering the drugs is to be considered. The usual dosage was one tablet three times a day, but the dosage can be increased up to two tablets three times a day if needed. During the whole period not one of the patients manifested any toxic reactions at all, nor in any case did the treatment have to be suspended for any reason.—I am, etc.,

Birmingham. ARTHUR HUSE.

REFERENCES

[1] *British Medical Journal*, 1947, **2**, 171.
[2] *J. Amer. med. Ass.*, 1940, **114**, 1334.

The Institute of Psycho-analysis

SIR,—There have recently appeared in the press statements which may lead to some embarrassment regarding the work of this Institute. The present building is too small for its teaching and clinical activities and its lease is near its end. Accordingly a new building has recently been purchased, but this cannot be ready for occupation for about a year, and therefore any expansion of the work of the Institute is not at the moment possible.—I am, etc.,

The Institute of Psycho-analysis, London, W.1. JOHN RICKMAN, President.

POINTS FROM LETTERS

Treatment of Obesity

Dr. JOSIAH OLDFIELD (London, W.1) writes: Dr. A. Lewis (if I understand his letter correctly) has discovered a safe and sure method for the rapid reduction of obesity (May 20, p. 1204). Without any drugs, without any reduction of fluid, without abstinence from salt, and without any rigid dieting, Dr. Lewis claims the ability to reduce patients pleasantly and safely at the rate of about 20 lb. in two or three months. May we be directed to Dr. Lewis's writings on this subject, or would he give a short synopsis of his methods?

Sulphonamides and Measles

Dr. C. DYSART (Bromley, Kent) writes: The following observations may not be original, but I should like to record my experiences in the use of a preparation containing sulphadiazine, sulphathiazole, and sulphamerazine in the treatment of measles. Over the past eighteen months I have treated 46 cases of measles with appropriate doses of this preparation. In two to four days both rash and bronchitis had cleared up remarkably. . . .

Unfair to Rabbits

Dr. R. S. SAXTON (Brighton) writes: Many innocent (and unlikely) methods of venereal infection have been thought out to explain V.D. in persons of irreproachable morals, but a new one of startling unlikelihood—not to say impossibility—is presented to readers of a popular weekly magazine. . . . Referring to health risks of consuming food that has not been subject to inspection by food officers, the article states, "That rabbit the motorist killed with his car may be full of V.D." The article in question, which is said to be by a "Public Health Officer," must surely have caused consternation among many of the magazine's more gullible readers. . . . I should be glad to hear of a plausible explanation of how one blames the rabbit.

Names of New Drugs

Dr. ROBERT DORMER (London, E.4) writes: I wish to indicate an important, but quite unnecessary, source of trouble to the profession. I refer to the similarity of names of new drugs. A representative list (of seven new drugs) contains 37 consonants. Thus, theoretically, each consonant in the alphabet could have been used 1.7 times. What has happened is as follows: L is used five times, P six times, and N twelve times, while the following consonants have not been used at all—B, F, J, K, Q, T, V, W, X, Y, Z. Is it not advisable that the makers of new words should look for their derivations to numerous languages besides ancient Greek?

Obituary

Dr. JOHN WATSON LITTLE, a well-known figure in West of Scotland medical circles, died suddenly on March 12 at his home in Newmains at the age of 74. He had been in practice in this busy industrial area of mid-Lanark for 47 years. A native of Glasgow, he graduated M.B., Ch.B. at the University there in 1897. After serving as a junior assistant at the Royal London Ophthalmic Hospital, he went into general practice. For over 40 years he was an active member of the British Medical Association, and he had acted as president of the Lanarkshire Branch. He was chairman of the Lanarkshire Division in 1934–5, and he served for many years on the Scottish Subcommittee and on the Insurance Acts Subcommittee for Scotland. He was also a justice of the peace for Lanarkshire. When the National Health Insurance Act was passed, Dr. Little was appointed a member of the Lanarkshire Panel Committee, and remained in office until the passing of the N.H.S. Act; for many years he was secretary of this committee. In 1912 the doctors of Lanarkshire formed the Lanarkshire Medical Practitioners Union, which in its time played an active part in medical politics in Scotland. Dr. Little was a member of the executive committee until its dissolution in 1949, and president for three years. At a dinner, held only two days before Dr. Little's death, Sir William Marshall spoke of the important work carried out by this group and made reference to Dr. Little's long and valuable service. Dr. Little was also one of the original members of the Colliery and Works Surgeons' Committee for Scotland, formed after the N.H.I. Act was passed to negotiate new terms of service with the Scottish Branch of the British Miners Federation. In all these organizations, he proved a sound counsellor and gave valuable service. For nearly 50 years he was keenly interested in first-aid work, and he was an honorary life member of the St. Andrews Ambulance Association. Dr. Little was a staunch and faithful member of the Church of Scotland and for many years an elder and manager of Coltness Memorial Church. He was active, too, in promoting good fellowship among doctors, and the Newmains area, with Little as secretary, was an object-lesson to other districts, the doctors there working in a close and amicable relationship, giving each a month's holiday a year and doing each other's work in illness and whenever necessary. Dr. Little was a fine type of kindly, capable, and experienced family doctor, who was regarded by his patients with the greatest respect and affection. He is survived by his widow, a married daughter, and a son who succeeds him in practice.—D. D. L.

Dr. JAMES PATRICK O'HEA, who died in Croydon on April 17 at the age of 82, was born in Cork, the elder son of the late Patrick O'Hea. He was a grandson of Dr. Woodforde and the great-grandson of the illustrious Dr. Henry Clutterbuck, who was seven times president of the London Medical Society. O'Hea was educated at private schools, at Cardiff University, and at St. Bartholomew's Hospital. He graduated M.B. in 1895, taking the F.R.C.S. a year later. He held resident appointments as a house-surgeon at the London Temperance Hospital and house-surgeon and later registrar at the Royal Eye Hospital. He became clinical assistant to the out-patient department of St. Bartholomew's Hospital, and much later he was one of the consulting neurologists to the Ministry of Pensions. During the 1914–18 war he joined the R.A.M.C. and served in hospital ships, in the Gallipoli campaign, and subsequently in prisoner-of-war camps. For a time after the war O'Hea was with the White Star Line as ship surgeon on the Australian and American routes before settling in private practice in Brixton. At the outbreak of the recent war he joined the Mercantile Marine as one of the medical officers of the Ellerman Line and he saw active service in the Mediterranean and other theatres of war, making his final trip to India when nearly 80 years old. James O'Hea was highly esteemed by his colleagues, not only for his tact and efficiency, but for his kindly nature and his sense of humour. He was charitable to a degree and very fond

of children. In his early days he wrote a book entitled *The Rearing of Children*, and he was also responsible for several articles on the care of children. Although of a shy disposition, this tribute was paid to him by the shipping line he served during the war: "He was regarded as a very fine shipmate by all hands—and this is the finest praise any sailor can give any man."

Dr. EDMUND CECIL SALT, who died in Burton-on-Trent on May 17, had been in failing health for some years. A son of the Rev. T. S. Salt, vicar of Curbar, Derbyshire, he was educated at Repton School and Cambridge, where he graduated B.A. in 1893 and M.B., B.Ch. in 1897. He was a student of the London Hospital and a contemporary of McAdam Eccles, who became his intimate friend. He served as house-surgeon and resident receiving-room officer at the London Hospital and later as assistant house-surgeon to the Poplar Hospital. In 1900 Salt returned to his native town of Burton-on-Trent, where his great-grandfather had been a founder of the brewing industry. There he went into partnership with the late Dr. Bridgman, and he continued in the same practice, with Dr. W. P. Lowe and later Dr. Frewer, until he retired in 1943. In 1902 he was appointed surgeon to the Burton Infirmary, and he remained in that post until his retirement, when he became consulting surgeon. Salt was a good general surgeon and his work in the infirmary was of a high standard. His whole interest was centred in his large and busy practice. He was the ideal general practitioner, kindly, cheerful, and never sparing himself. His services were in great demand and he endeared himself to a host of patients. He was devoted to golf—his only recreation—but he got little time for it except during his annual holiday, which he regularly spent in Scotland at his beloved Machrihanish. Dr. Salt was a man of deep Christian faith, and his services to the community as doctor and friend will long be remembered. He is survived by his widow and two married daughters.—W. W. G.

Dr. HAROLD WARBURTON LEWIS, of Newbury, died on May 26 at the age of 56. He was the son of the Rev. John. E. Lewis, of Brierley Hill, Staffordshire, and was educated at Kingswood School, Bath. At the outbreak of war in 1914 he was a medical student at the Middlesex Hospital, and immediately volunteered for service with the ambulance unit organized by the Duchess of Sutherland. After serving for several months he returned in 1915 to his medical studies, and on qualifying in 1917 he was commissioned in the R.A.M.C. He served in France, Mesopotamia, and Kurdistan, and on demobilization went into practice at Redditch after he had graduated M.B., B.S. in 1921. In 1929 he joined the late Dr. E. S. Hemsted, who had undoubtedly the busiest general practice in the Newbury locality. Here he quickly settled down as Dr. Hemsted's right-hand man, and soon his reputation was little, if at all, short of that of his senior partner. Both were hard workers, and Lewis's bent for surgery led to his undertaking many responsibilities at the Newbury Hospital. During the war Dr. Fletcher, who had been taken into the firm as junior partner, went on military service. Dr. Hemsted was already advanced in years, and so a great extra strain was thrown on Dr. Lewis, who never spared himself in responding to the heavy calls made upon him. It is said that the only "time off" he had during the whole of the 1939–45 war was about four or five week-ends. Last year his health broke down, and quite recently he had at last bowed to the inevitable and retired from practice. Dr. Lewis is survived by his widow and three children; one son, Dr. John Lewis, followed his father's profession.

Dr. JOHN KEITH CUMMING died on May 28 in the Royal Infirmary, Blackburn, where he was senior consultant surgeon. His sudden and unexpected death came as a great shock to his colleagues and many friends throughout East Lancashire. The elder son of Dr. Robert Cumming, of Great Harwood, he was educated at Giggleswick and Aberdeen University, graduating M.B., Ch.B. in 1922. He was house-surgeon at the Aberdeen Royal Infirmary to the late Sir Henry Gray, later acting as his private assistant for a time. Cumming had an abiding respect and affection for Sir Henry, and there is little doubt that this association first inspired in him a love for surgery. Joining his father in practice in 1923, Cumming became honorary anaesthetist to the Blackburn Royal Infirmary in 1924, and assistant surgeon four years later. It was then that he embarked upon many years of hard and unremitting work in the out-patient department, and in the surgical wards and theatre. Although this afforded him vast experience it yielded him very little financial reward. As assistant to R. Y. Aitken, the senior surgeon, Cumming gained the sound grounding in all branches so essential to a general surgeon. In 1930 he was put in charge of the radium clinic and in 1932 became full surgeon to the hospital. An active member of the B.M.A., he was chairman of the Blackburn Division in 1947–8. He was a keen member of the Blackburn Medical Society and of the Manchester Surgical Society, and rarely missed a meeting of either. He particularly enjoyed the occasional opportunity to visit leading centres in the North to attend surgical conferences. During the war years, when the consulting obstetrician was called up, Cumming, along with a colleague, Mr. C. M. Pearce, undertook the emergency obstetric work for the Blackburn area. This, on top of his private and hospital work at the Royal Infirmary and at Queens Park Hospital, was a heavy burden which he bore unflinchingly and uncomplainingly until 1945. There is no doubt that these years of arduous duties, with rarely a whole night in bed, told heavily upon his constitution, for in recent years he lacked his former energy. In 1945 he abandoned general practice to devote himself to surgery. Dr. Cumming was married in 1940 to Miss Margaret Broadley.—A. L. McA.

Dr. HUGH ALTON CHANDOS WALL, who died recently, graduated M.B., Ch.B. at the University of Sydney in 1915. Soon afterwards he was one of those many Dominion doctors who enlisted. He was with the B.E.F., and he served in Gallipoli, being invalided back to Australia from Lemnos. On his return he was appointed to St. Vincent's Hospital, Sydney, where he became house-surgeon to Sir Alexander MacCormack. His health improving, he again saw service, this time as a surgeon-lieutenant, R.A.N., being appointed M.O. to the Australian destroyer flotilla sweeping for Austrian submarines in the Adriatic, and based on Brindisi. He later went into practice on the north coast of New South Wales.—K. B.

ROBERT MENZIES GALLOWAY, medical officer of health of Bolton, died at the Townleys Hospital on June 5, at the age of 51. Born in Birkenhead, he received his early education in England and went to Edinburgh for his medical education, graduating M.B., Ch.B., with honours in 1920. His academic career was interrupted by service as a surgeon probationer in the 1914–18 war. Galloway spent his first five years after qualifying in hospital appointments and thus laid a solid foundation for his future career. He took his D.P.H. in Manchester in 1923 and two years later proceeded M.D. with commendation. His apprenticeship in the public health service was by way of appointments as assistant in Bolton and with the Lancashire County Council under two pioneers, the late Paget Moffat and Dr. Butterworth. In 1929 he became medical officer of health of Dewsbury and three years later he went to Bolton as medical officer of health there. He was a sound doctor and at the same time an administrator of no mean ability and acumen. For these reasons, quite apart from his worth as a man, he was held in high esteem not only by his authority but also by his colleagues and those members of the public health service who were privileged to enjoy his friendship. His fondness for children and young people found expression in his work for the Bolton Lads' Club. Galloway received many honours. He was a fellow and examiner of the Royal Sanitary Institute, of which body he was also a member of council. He was a Fellow of the Society of Medical Officers of Health and had been president of the North West Branch. Only last year, as president of the County Borough Group, he met his fellow members in a delightful and memorable week-end at Windermere. As recently as 1948 he was appointed lecturer in public health at Manchester University. The influence of his education in Scotland, where he spent many of his early holidays, was reflected in a pawky yet kindly and whimsical humour. As a

raconteur he was in great demand. His intimate knowledge and understanding of his fellow men could be expressed with equal fluency in the Lancashire dialect, broad Scots, Welsh, or even Irish. Both as a man and as an outstanding medical officer of health he will be mourned, and to his widow and four children the sympathy of his friends and colleagues will be extended. His elder daughter is due to qualify soon at Edinburgh, while his elder son is in his second year at Cambridge.—J. Y., V. T. T., H. M.

Dr. MORRIS BENJAMIN BRODY, who died some months ago in Sheffield at the age of 37, was outstanding as a clinician and as a scholar. A native of Sheffield, he graduated M.B., B.Ch. with honours at Sheffield University at the age of 21, proceeding M.D. in 1941. He took the D.P.M. in 1937. After holding a number of house appointments he joined the staff of Runwell Hospital, where he worked for nine years. During this period he established himself not only as an excellent psychiatrist of unusual versatility but also as a research worker of great promise. His important studies on mental testing in the dementias and major psychoses are well known to psychiatrists and psychologists. He also made valuable contributions to the testing of patients after leucotomy and to the problem of social psychotherapy. From 1946 he was working at Graylingwell Hospital, Chichester, first as a senior psychiatrist and deputy superintendent and lately as director of research. His tireless energy, his great knowledge, his therapeutic optimism, and his enthusiasm as a teacher contributed greatly to the reputation of the hospital. Although still young as a specialist, he was elected a member of the council of the Psychiatric Section of the Royal Society of Medicine. He was also honorary secretary of the Clinical Psychiatry Subcommittee of the Royal Medico-Psychological Association. Dr. Brody was regarded as one of the most gifted among the younger British psychiatrists. Personally he was of youthful charm, always cheerful and witty, and often profound. His tragic death from malignant disease will be mourned by everybody who had the privilege of knowing him. He is survived by his widow and two sons.—E. S.

Dr. WILLIAM FREEMAN SNOW, who was chairman of the board of directors of the American Social Hygiene Association and president of the Union Contre le Péril Vénérienne, died on June 12.

Medico-Legal

SULPHATHIAZOLE PATENT REVOKED

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

In 1937 the manufacturing firms Messrs. May and Baker, Limited, and Ciba, Limited, discovered how to make sulphathiazole and sulphamethylthiazole by incorporating certain groups in the sulphanilamide molecule. They were jointly granted letters patent for these inventions. In September, 1946, Boots Pure Drug Company, Limited, presented a petition for revocation of the patent on the grounds that it was unduly wide. This petition was granted in January, 1948, by Mr. Justice Jenkins, who found that, although the drugs were useful and their production was a patentable invention, the claims of the specification included all sulphathiazoles whether or not an additional atom or group was joined to the sulphanilamide or thiazole portion of the molecule. This was an extremely large class and the claim would have covered many millions of products. He also refused a motion by the patentees to be allowed to amend their specification so as to claim only the manufacture of the two substances to which it specifically referred.

They then appealed to the Court of Appeal, which held that the specification as amended would claim an invention substantially different from that claimed originally, and therefore dismissed the appeal. Subsequently the House of Lords, by a majority decision, arrived at the same conclusion.[1]

Lord Simonds said, in his opinion, that in the original specification there was no hint that the exemplary drugs sulphathiazole and sulphamethylthiazole were essentially distinguishable from any other members of the vast group within which they fell, or that they had some peculiar characteristic which gave them a therapeutic value. No one could fairly read the specification without concluding that their therapeutic value was derived from a generic quality. They illustrated the invention just because they had that quality. No separate claim was made for the manufacture of those two specific drugs, or for the drugs themselves, or either of them. The appellants had maintained that they could not be claiming a substantially different invention, because they were limiting the claims of their specification to the only form of the invention specifically described and claimed in general terms in the unamended specification. His Lordship thought, however, that it was begging the question to say that, in every case in which the patentee had stated the nature of his invention in wide and general terms and then given an illustration of it, he could shift his ground and claim that his invention was not the general but the particular. He could do so only if they were the same invention. The proposed amendment would make the invention claimed substantially different from that claimed before amendment and was therefore not permissible under the Act. He therefore dismissed the appeal, and Lord Normand and Lord MacDermott agreed.

Lord Morton, however, thought that the proposed amendment was by way of a disclaimer and hence admissible under the Patents and Designs Acts. The two drugs were the preferred embodiment of the invention described in the specification, and the patentees were claiming in the amendment something which was not a substantially different invention but part of the wide invention originally claimed.

Lord Reid also thought that the proposed amendment was competent. The majority judgment, however, deprived Messrs. May and Baker, Limited, and Messrs. Ciba, Limited, finally of their patent on these drugs.

[1] *The Times*, February 10, 1950.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

In Congregation on May 27 the honorary degree of M.A. was conferred on Wilfrid Paton Philip, M.B., Ch.B., D.P.H., D.M.R.E.

The following medical degrees were conferred on May 27:

M.D.—R. N. R. Grant, Vivien U. Lutwyche.

M.CHIR.—*H. E. Lockhart-Mummery.

M.B., B.CHIR.—Mrs. Margaret M. Bates.

*By proxy.

Dr. H. M. Evans, Director of the Institute of Experimental Biology in the University of California, will deliver a lecture on "Hormones and the Anterior Pituitary Gland" in the theatre of the Biochemical Laboratory on Monday, September 4, at 3 p.m. The lecture is open without fee to all members of the University.

UNIVERSITY OF EDINBURGH

David Whitteridge, D.M., has been appointed Professor of Physiology in the University of Edinburgh in succession to the late Professor W. H. Newton. Professor Whitteridge, who is aged 38, graduated with the Oxford degree in 1937 after doing his clinical training at King's College Hospital, London, and proceeded D.M. in 1946. He was appointed demonstrator in physiology at Oxford in 1938, and was awarded a Beit Memorial Research Fellowship in 1940; he was also appointed a Schorstein Research Fellow. He has worked mainly on the physiology of the nervous system, and is senior secretary of the Physiological Society.

UNIVERSITY OF LONDON

The following candidates have been approved at the examination indicated:

THIRD M.B., B.S.—[1 3]F. L. Ashworth, [1 3]H. M. Baird, [1 3]M. O. J. Bewers, [1 5]W. J. D. Bradfield, [1 5]Gladys V. Bradshaw, [1 3]A. E. R. Buckle, [1 7]Mary G. Eldridge, [1 2 4 5 7]M. P. W. Godfrey (*University Medal*), [1 5]E. M. Jepson, [1 7]W. E. Miall,

[1 4]Margot L. S. Norton, [1 5]J. H. Owen, [1 6]R. A. Parkins, [1 4]J. B. Parsons, [1 4]J. E. H. Pendower, [1 2]Theresa Posner, [1 2 3]A. E. A. Read, [1 2 3]A. F. Wallace, H. R. Alderton, Anne M. Allen, M. J. Allwood, D. W. Anniss, J. H. Apted, R. Armatage, J. H. Armstrong, Doreen R. Austin, Margaret A. Austin, Pamela M. Bacon, Sybille Baer, H. Barkley, H. Barrie, Mary Bateman, G. R. Benett, P. F. Benson, J. A. Bloomfield, Joyce O. M. Board, Marie J. Bouton, Christine A. Bratt, B. I. Brest, W. Brooks, F. J. Brunton, A. C. Bryan, J. B. G. Burke, J. I. Burn, T. V. Campkin, L. H. Capel, N. S. Capstick, D. M. Carnegie, J. C. B. E. Carreras, J. T. Cecil, D. G. Chalmers, G. E. Chorley, J. A. Churcher, J. H. Comty, M. B. Conran, E. H. Cooper, June P. Cooper, J. T. Cope, M. P. Coplans, J. G. Corson, Margaret E. Cowan, R. E. Cowling, J. S. Cox, A. A. Craigen, R. Q. Crellin, R. J. Cremer, Maureen N. Currie, Eluned B. Davies, E. R. Davies, R. G. Davies, R. A. L. Davis, K. R. J. de Belder, L. R. De Jode, F. L. A. de Marneffe, L. R. Dennis, G. K. M. Drown, R. V. Dugdale, P. G. J. Duncan, H. Duschinsky, D. N. Edwards, F. G. Ellis, G. J. Evans, F. H. Evason, J. R. Eve, M. B. Fell, Margaret D. Findlay, M. H. Flint, A. T. T. Forrester, Jean E. François, A. F. Franks, E. H. Franks, J. Fraser, A. E. Fyfe, I. T. Gabe, Frances F. Gibbs, Jean Gillbard, W. V. Graham, A. H. Gray, P. C. W. Greaves, N. A. Green, R. C. Greenberg, Katherine Grice, H. E. D. Griffiths, D. J. Grimsdell, Jean E. Griswood, J. S. Hales, H. FitzA. Hamilton, R. R. M. Harman, Ruth F. Harris, T. S. Hart, P. M. Healy, K. R. Heber, B. J. Helyer, K. M. Hewitt, B. M. Hibbard, K. Higgins, Frances M. Hill, L. Hinton, W. G. Holland, G. W. Howard, J. B. Ll. Howell, D. C. Hughes, J. W. Hughes, S. Hulme, J. A. Hunt, D. G. Hurter, J. P. Jackson, A. Ll. Jeanes, H. G. Jeffs, A. V. Jenkins, I. G. Johnston, D. M. Jones, Eleanor M. Jones, E. Ll. Jones, M. A. Kalina, M. Kaye, Patricia M. Keefe, G. Keen, P. W. L. Kelly, C. H. Kendall, N. B. Kreitman, S. T. Langham, F. W. Lapage, G. A. Lawrence, J. Lawson-Matthew, P. J. Lawther, Stephanie M. Leese, Gweneth M. Leigh, J. C. Leonard, A. P. R. Lewis, E. C. Lewis, T. D. Lewis, W. R. Little, Eunice Lockey, R. L. Luffingham, M. A. Macan-Markar, D. O. N. McIntyre, T. A. Marmion, M. K. Mason, Pamela G. L. W. Mason, R. J. P. Melvin, Sheila C. S. Meux, R. C. Michell, G. G. M. Miles, J. B. Millard, R. E. Molloy, Patricia A. Monk, G. J. M. Moore, D. J. Ll. Murphy, T. O. na Oruwariye, Eileen M. Newton, D. S. Noble, L. I. Norman, Patricia L. Obee, R. H. Oldfield, T. M. Owen, J. B. Parton, J. A. Payne, D. J. Pearce, L. H. Pell, F. J. C. Perera, L. E. Perkins, Anne M. Phillips, G. F. M. Pierce, Isabel M. Pine, F. R. M. M. Prat, J. L. Price, C. O. M. Priday, Suzanne L. Quittner, A. M. Reader, J. H. Rees, B. G. Reynolds, D. McL. Riddell, A. W. Roberts, F. L. Roberts, Margaret G. Roberts, E. Roderic-Evans, Thea G. T. Rose, M. Rosenfeld, N. G. Rothnie, T. I. Rowland, D. Rowley, D. J. Rudman, Stella Salt, Elizabeth B. Samson, Barbara E. Schooling, Diana M. Scott, I. A. W. Scott, K. C. Searle, A. B. Seth-Smith, R. N. Sidebotham, P. H. Simmons, P. A. Skinner, A. L. Slater, H. C. Smellie, B. O. Smith, D. S. M. Smith, Margaret F. Smith, R. V. Smith, Mary Soppitt, P. R. Sowerby, P. B. Sparke, N. E. Stebbings, Janet M. Stokes, G. J. Stopps, J. D. Studdy, D. E. Sturdy, J. C. Sumption, G. P. Tannen, Susanne M. Tauber, A. R. Taylor, Felicia D. Thomas, Gwendolen M. G. Thomas, M. G. Thompson, Eleanor M. R. Till, M. G. S. Vercoe, A. J. Wainwright, J. C. N. Wakeley, Cecilia M. Ward, P. Ward, P. F. M. Warlow, P. K. G. Warren, Paula M. Watkin, Mary D. Watkins, R. W. W. Watson, W. H. Watson, Sheila M. Watts, Josephine P. Werren, A. E. Wheatley, Margaret White, A. Wiener, H. N. S. Wilkinson, Evelyn M. Williams, T. C. P. Williams, V. A. Wills, M. R. Witney, J. C. Woolf, D. E. Wright, D. A. Wright, I. W. M. Wright, R. Zakon.

[1]With honours. [2]Distinguished in pathology. [3]Distinguished in hygiene and forensic medicine. [4]Distinguished in medicine. [5]Distinguished in applied pharmacology and therapeutics. [6]Distinguished in surgery. [7]Distinguished in obstetrics and gynaecology.

The governing body of the British Postgraduate Medical Federation has awarded postgraduate travelling fellowships for 1950–1, tenable for one year, to G. L. W. Bonney, M.S., F.R.C.S., of the Institute of Orthopaedics (orthopaedic surgery, Manchester and Scandinavia); P. J. Hare, M.B., M.R.C.P., of University College Hospital (dermatology, France and Switzerland); H. O. Jones, M.S., F.R.C.S., of King's College Hospital (thoracic surgery, Leeds and Scandinavia); J. S. Pegum, M.B., M.R.C.P., of Guy's Hospital (dermatology, France and Switzerland); and D. J. Robertson, F.R.C.S., of St. Bartholomew's Hospital (vascular surgery, Edinburgh and Scandinavia).

UNIVERSITY OF WALES

The following candidates at the Welsh National School of Medicine have satisfied the examiners at the examination indicated:

TUBERCULOUS DISEASES DIPLOMA.—L. B. Banerjee, S. K. Gangopadhyay (with distinction), K. A. Goh, Y. R. Joshi, C. Y. Lien, R. N. Mukerjee, P. K. Murphy, J. K. Nag, M. L. Rahman, V. S. Rao, Gwenith E. Sibthorpe.

UNIVERSITY OF BIRMINGHAM

On May 4 and 5 the University of Birmingham celebrated the fiftieth anniversary of the granting of its charter on March 24, 1900. The celebrations included a dinner on May 4 and a degree Congregation, a luncheon, and a reception on May 5. At the Congregation on May 5 Princess Alice, Countess of Athlone, who proposed the toast of the University at the dinner on May 4, was the recipient of the honorary degree of LL.D., and Francis Brett Young, M.B., Ch.B., received the honorary degree of D.Litt. Mr. Anthony Eden, P.C., Chancellor of the University, proposed the toast of the honorary graduates at the luncheon held by invitation of the Guild of Graduates on May 5, and the American Ambassador, Mr. Lewis Douglas, who received the honorary degree of LL.D., proposed the toast of the Guild. At the reception on May 5 the guests were received by the Chancellor and the Pro-Chancellor.

UNIVERSITY OF LIVERPOOL

The following candidates have been approved at the examination indicated:

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—B. O. Barry, T. Briceno-Maaz, L. H. Chandler, C.-S. Chou, E. W. R. Fairley, D. E. Freeman, J. B. Henderson, L. H. Holroyd (recommended for the Milne Medal in Tropical Medicine), A. W. Iljon, C.-L. Lee, T. P. Niyogi, A. B. Raper (recommended for the Warrington Yorke Medal in Tropical Hygiene), D. K. Sen, K. C. Trivedi, A. F. Tuboku-Metzger, C. E. M. Wenyon.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College held on June 8 the following hospitals were recognized under paragraph 23 of the Fellowship regulations: King Edward Memorial Hospital, Ealing, house-surgeon to senior surgeon, gynaecologist and deputy resident surgical officer (for six months), senior officer to orthopaedic department (for six months), house-surgeon to a general surgeon and the oto-laryngologist (for six months) (to be recognized for general surgery only); Pembury District Hospital, Tunbridge Wells, first and second house-surgeons (for 12 months), orthopaedic registrar and orthopaedic house-surgeon (each for six months).

The following were co-opted to the Council for the year 1950–1 representing various branches of practice: *General Practice*, Dr. H. Guy Dain; *Gynaecology and Obstetrics*, Professor A. M. Claye; *Oto-Laryngology*, Mr. V. E. Negus; *Anaesthetics*, Mr. A. D. Marston; *Ophthalmology*, Mr. J. H. Doggart; *Dental Surgery*, Professor R. V. Bradlaw; *Radiology*, Professor B. W. Windeyer.

The title of the Hunterian Lecture to be given at the College (Lincoln's Inn Fields, London, W.C.) on Tuesday, June 27, at 5 p.m., by Dr. Arthur W. Allen has been changed to "Current Trends in the Surgical Management of Lesions of the Colon."

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

The following Members were admitted to the Fellowship of the College on June 2: M. L. Abrahamson, R. G. Cross, F. F. Kane, S. Sevitt.

On the same date the following were admitted to the Membership: D. V. Doshi, A. A. McG. McConnell, R. V. Rele, C. M. Sheridan.

The Services

Major-General J. M. Macfie, C.B.E., M.C., late R.A.M.C., has been appointed Honorary Surgeon to the King, in succession to Major-General R. W. Galloway, C.B., C.B.E., D.S.O., late R.A.M.C., retired.

Brigadier R. D. Cameron, C.B.E., M.C., late R.A.M.C., has been appointed a Director of Medical Services, and has been granted the temporary rank of Major-General.

The board of management for the Greenock and District Hospitals is to erect a new block of 64 beds at Larkfield Hospital, Greenock, for general medical patients. The design will be based on the work of a team sponsored by the Nuffield Provincial Hospitals Trust, which is at present carrying out research into the function and design of hospitals. It is hoped that the work of construction will begin in the spring of next year.

No. 21

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended May 27.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1950					1949 (Corresponding Week)				
	(a)	(b)	(c)	(d)	(e)	(a)	(b)	(c)	(d)	(e)
Meningococcal infection	40	2	19	1	1	34	6	22	—	1
Deaths		—	1				—	—		
Diphtheria	60	3	19	6	2	92	10	27	3	5
Deaths	—	—	—	—	—	—	—	—	—	—
Dysentery	457	15	111	2	2	55	5	19	1	1
Deaths					—				—	—
Encephalitis, acute	4	—	—		—	—	—	2	—	—
Deaths		—		—						
Erysipelas			24	3	3			27	3	5
Deaths							—			
Infective enteritis or diarrhoea under 2 years				24					41	
Deaths	17		2	2	1	12	1	3	3	—
Measles*	9,354	463	725	224	178	8,478	1105	480	194	183
Deaths†			1	—	—			—	—	—
Ophthalmia neonatorum	50	3	4		—	47	1	3	1	—
Deaths										
Paratyphoid fever	5	—	—	1 (B)	—	8	—	1 (B)	—	—
Deaths	—		—		—	—	—	—	—	—
Pneumonia, influenzal	489	20	7	—	6	441	24	7	6	10
Deaths (from influenza)‡	17	2	1	—	—	19	2	2	2	—
Pneumonia, primary			166	¶				197	34	
Deaths	167	22		9	6	164	29		5	9
Poliomyelitis, acute	50	5	7	5	5	12	1	3	1	1
Deaths§	3	—		—		—	—			
Puerperal fever		—	7				—	9		
Deaths										
Puerperal pyrexia‖	82	8	4		2	86	10	7	3	1
Deaths							—			
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	1,295	104	167	84	71	1,108	70	137	56	31
Deaths†			—	—	—			—	—	—
Smallpox	—	—	—		—	3	—	—	—	—
Deaths					—				—	—
Typhoid fever	6	—	3	4	—	4	1	—	2	—
Deaths	—	—	—		—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths					—				—	—
Whooping-cough	2,966	172	372	79	45	2,824	155	201	159	71
Deaths	5	—	1	—	—	12	1	—	2	—
Deaths (0–1 year)	228	27	26	12	10	264	36	28	18	6
Deaths (excluding stillbirths)	4,558	698	587	177	98	4,491	686	533	185	129
Annual death rate (per 1,000 persons living)			11·8					10·7	11·5	
Live births	7,363	1191	955	457	234	8,295	1355	1058	430	251
Annual rate per 1,000 persons living			19·2					21·2	26·6	
Stillbirths	178	14	27			191	24	25		
Rate per 1,000 total births (including stillborn)			27					23		

* Measles is not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales. London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

¶ Primary pneumonia no longer notifiable in Eire.

EPIDEMIOLOGICAL NOTES

Discussion of Table

In *England and Wales* there were increases in the notifications of measles 526, scarlet fever 118, dysentery 66, and acute poliomyelitis 25, with decreases in the incidence of whooping-cough 271 and acute pneumonia 105.

The largest increases in the notifications of measles were: Warwickshire 159, Middlesex 117, London 97, and Essex 78; the largest exceptions to the general trend were falls in Norfolk 89 and Suffolk 80. The chief feature of the incidence of diphtheria was a rise of 5 in Durham. Variations in the trends of scarlet fever were small; the largest were increases in the notifications in Kent 31 and Essex 30. The decline in the incidence of whooping-cough was largely due to the experience of Yorkshire West Riding, where 140 fewer cases were notified than in the preceding week.

The rise in the incidence of acute poliomyelitis was confined to two areas, Warwickshire, Birmingham C.B. 10 and Staffordshire 10 (Stone R.D. 5 and Rowley Regis M.B. 3).

The largest returns of dysentery were: Yorkshire West Riding 169 (Sheffield C.B. 37, Bradford C.B. 30, Queensbury and Shelf U.D. 25, Dewsbury C.B. 19, Rotherham C.B. 13, Thorne R.D. 9); Lancashire 79 (Manchester C.B. 22, Oldham 15, Preston C.B. 14); Durham 70 (Stanley U.D. 21, South Shields C.B. 17, Ryton U.D. 10); London 15 (Lewisham 6); Surrey 12 (Reigate M.B. 6); Gloucestershire 11 (Thornbury R.D. 7); Yorkshire East Riding 10 (Kingston-upon-Hull C.B. 10).

In *Scotland* there were increases in the notifications of scarlet fever 51 and measles 37, with decreases in the incidence of whooping-cough 16 and dysentery 10. The incidence of scarlet fever rose throughout the country. The largest returns of dysentery were Glasgow 70, Dundee 18, and Edinburgh 13. Notifications of diphtheria in Glasgow rose from 5 to 14, while a fall was recorded in the remainder of the country.

In *Eire* increases were recorded in the notifications of scarlet fever 26 and whooping-cough 20, while a decrease of 55 was reported for measles. Although the total notifications of measles declined a rise of 23 occurred in Dublin C.B. The rise in the incidence of whooping-cough was contributed by Kilkenny, Waterford No. 2 R.D., where there was an outbreak with 39 notifications.

In *Northern Ireland* a decrease of 58 in the notifications of measles was the only change of any size in the trends of infectious diseases. This fall was mainly due to the experience of Belfast C.B.

Week Ending June 3

Notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,158, whooping-cough 2,613, diphtheria 45, measles 10,075, acute pneumonia 458, acute poliomyelitis 37, dysentery 454, paratyphoid fever 5, typhoid fever 3.

Medical News

National Foot Health Week

A "National Foot Health Week" was inaugurated on June 12 in the form of a campaign in London and large industrial centres to call attention to the ill-health caused by the wearing of ill-fitting shoes, particularly during childhood. A four-day exhibition at Westminster Central Hall was opened by Sir Wilson Jameson, who spoke of the importance of co-operation between doctors and scientific workers on the one hand and those engaged in the shoe industry on the other. It was now beginning to be appreciated, he said, that if we did not walk or stand or sit in the proper fashion, whether through carelessness or ignorance or some anatomical defect, strain was thrown on the whole body and efficiency was markedly impaired. Modern life had greatly accentuated conditions adverse to foot health. Walking was undertaken to a very much less degree than formerly, and

many workers, including women, had to stand for long hours on hard surfaces. Child-welfare and school medical services had existed for more than thirty years, but in neither of them had enough attention been paid to the condition of the children's feet or to their footwear. He was a school medical officer himself at the time when the medical inspection of secondary school children was introduced, and he found more serious foot defects than he had thought possible, but he was ill-equipped at that time to deal adequately with them. Medical men were now in a better position to give good advice, but information was still insufficient, and there was inadequate appreciation in the medical profession itself of the need for education in relation to the foot. Mr. F. H. Bentley, director of the Foot Health Educational Bureau, said that it was all to the good that the medical profession was now studying the foot in relation to the shoe instead of as a static structure. The programme of the exhibition included lectures by members of the medical profession and others, shoe-fitting demonstrations, and conferences and question forums. The public were shown how to care for their feet and their footwear, and there was a special section dealing with hosiery and another showing how shoes are made. The results of a survey carried out in the West Riding by the shoe trade research association were exhibited. Of one thousand children whose feet were examined, two-thirds were found to have shoes which were too short—the most common of all faults. The historical side of the exhibition was also interesting, and it must have come as a surprise to many visitors to learn that as recently as one hundred years ago many people wore shoes known as "straights," the right and the left being interchangeable.

Mark of Appreciation

Students who attended the courses for the Diploma in Public Health at the London School of Hygiene during the years 1929–39 gave a dinner at the Savoy Hotel on June 9 to Sir Wilson Jameson and Brigadier G. S. Parkinson. Sir Wilson, who was dean of the school and professor of public health, and Brigadier Parkinson, who was vice-dean (and dean for a period during the war), retired from their posts at a time in the war when it was impracticable for old students to mark their appreciation of what these two did for those entering the public health service. The opportunity was therefore taken to hold the dinner on the occasion of Sir Wilson's retirement from the post of Chief Medical Officer at the Ministry of Health. A third guest at the dinner was Miss K. M. Shaw, well known to all old students at the school. As a memento of the occasion Sir Wilson Jameson and Brigadier Parkinson were each presented with a volume containing the signatures of over 200 of the students who attended D.P.H. courses during 1929–39. The beautiful binding in hand-tooled leather was the work of Mr. Anthony Gardner.

Visitor from Pakistan

Dr. Q. M. Said, secretary of the Institute of Hygiene and Preventive Medicine, Lahore, is visiting Britain for six weeks under the auspices of the British Council. He has been attending the World Health Organization's congress at Geneva, and he has come here to study public health services, particularly in rural areas, and the work being done in the field of preventive medicine. Dr. Said studied at the London School of Hygiene and Tropical Medicine from 1925 to 1927, and on returning to the Punjab was appointed a district medical officer of health. In 1949, as assistant director of public health for the Punjab, he submitted a report as the result of which the institute at Lahore was formed.

Delinquents in Denmark

A film on the treatment of mentally abnormal delinquents at Herstedvester, Denmark, was shown at the French Institute on June 6 under the auspices of the Institute for the Scientific Treatment of Delinquency and the Howard League for Penal Reform. The institution of Herstedvester receives about 2% of those criminals who are sentenced to terms of imprisonment of six months or more or against whom special precautions are taken. The film illustrated the daily routine of life in the institution, and in particular traced the history of one of its inmates. Dr. G. K. Stürup, who is superintendent of the institution, was present at the film show, and explained some points of interest. At present the institution treats nearly 300 inmates compared with 150 when it was opened in 1935. A further 200 are on parole and under supervision from the institution. Danish methods differ in two main respects from British: first, sentences of indeterminate length are given, and secondly some of the inmates submit to sterilization or castration. According to Dr. Stürup most of the inmates are not worried by the indeterminate sentence, and he believes that it is necessary for their proper treatment. Castration is thought to be distinctly beneficial for certain types of criminals who have committed sexual offences. About 48% of the inmates are sexually abnormal, 8% psychotic, 8% epileptic, 26% mentally retarded, and 23% neurotic (these categories are not mutually exclusive). Of the first 300 patients only 12 are still in the institution, 8 are dead, and 22 have been transferred to mental hospitals or institutions for mental defectives.

Lady Tata Memorial Trust

The trustees of the Lady Tata Memorial Fund announce that, on the recommendation of the Scientific Advisory Committee in London, they have made the following awards for research in blood diseases, with special reference to leukaemia, in the academic year beginning on October 1, 1950: *Grants for research expenses and assistance*, Professor Jörgen Bichel (Denmark), for work at Aarhus, Denmark; Dr. George Discombe (Great Britain), for work in London; Dr. Astrid Fagraeus and Dr. Bo Thorell (Sweden), for work in Stockholm; Dr. Niels Gunnersen Harboe (Denmark), for work in Copenhagen; Dr. Endrev Kelemen (Hungary), for work at Szeged; Professor Charles Oberling (France), for work in Paris; Dr. Edith Paterson (Great Britain), for work at Manchester; Dr. Günther Schallock (Germany), for work at Münster. *Scholarships*, Dr. Pascou Atanasiu (Rumania), for work in Paris; Dr. Henri Paul Lucien Febvre (France), for work in Paris.

W.H.O. Executive Board

Dr. H. S. Gear, of South Africa, has been appointed chairman of the Executive Board of the World Health Organization.

Society of Medical Officers of Health

Dr. J. M. Gibson, medical officer of health for Huddersfield, has been appointed president of the Society of Medical Officers of Health in succession to Dr. H. C. Maurice Williams. He takes office on October 1.

Memorial Fund

It has been suggested that a fund should be created to give enduring recognition to the services of the late Professor T. P. McMurray, who by his skill as a surgeon and a teacher enhanced a great tradition. With the object of perpetuating his memory it is proposed to raise a memorial fund, to be offered to the University of Liverpool for the establishment of a prize for clinical work in orthopaedic surgery to be associated with the name of T. P. McMurray. Contributions may be sent to Mr. Bryan McFarland, Department of Orthopaedic Surgery, the University, Liverpool.

Wills

Mr. John Philip Buckley, of Manchester, left £94,315. Dr. Frank Husband-Clutton, formerly medical officer for the Crowland district of Peterborough, left £77,211; Dr. Mina Louisa Dobbie, of Bournemouth, £14,616; and Dr. Norman Cumming Rogers, of St. John's Wood, London, £5,711. Dr. Cecil Clifford Dobell, formerly protistologist to the Medical Research Council, left £14,055; and Mr. Joseph Edwin Barnard, formerly director of the department of applied optics at the National Institute for Medical Research, £58,520.

COMING EVENTS

Industrial Health

The third Mackenzie Industrial Health Lecture, given under the auspices of the B.M.A. in conjunction with the Association of Industrial Medical Officers, will be delivered by Professor R. E. Lane on Wednesday, June 28, at 2.30 p.m. in the Main Hall, Nuffield House, Queen Elizabeth Hospital, Birmingham. His subject is "Education and Industrial Health." Admission is free.

Contraceptive Technique

A lecture and demonstration (on living models) on contraceptive technique will be given by Dr. Marie Stopes at the Mothers' Clinic, 108, Whitfield Street, London, W., on Thursday, July 6, at 2.30 p.m. **Tickets must be obtained in advance,** as accommodation is limited.

Hospital Administrators

The Institute of Hospital Administrators will hold a Summer School on July 1–28 at High Leigh, Hoddesdon, Herts. Full particulars may be obtained from the Director of Education, Institute of Hospital Administrators, Tavistock House North, Tavistock Square, London, W.C.1.

Renal Association

The second general meeting of the Renal Association will be held at the Ciba Foundation, 41, Portland Place, London, W., on Wednesday, June 21, at 4 p.m.

Tropical Hygiene for Laymen

The Ross Institute of Tropical Hygiene will hold its annual course in tropical hygiene for planters and miners on July 24–28. There is no fee for the course. Full particulars may be obtained from the organizing secretary at the London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1.

Course for General Practitioners

The National Temperance Hospital will run a postgraduate course for general practitioners on July 3–8. Particulars may be obtained from the hospital at Hampstead Road, London, N.W.1.

Gastro-enterology in Brazil

The Second Pan-American Congress of Gastroenterology will be held at Rio de Janeiro and São Paulo, Brazil, on July 23–29 under the auspices of the Inter-American Association of Gastroenterology. Particulars may be obtained from the Secretaria Geral, Rua 7 de Abril, 176, São Paulo, Brazil.

Congress at Verona

Papers on many aspects of medicine will be read at a Congress—the Giornate Mediche Internazionali—to be held at Verona on July 20–30. Particulars may be obtained from Professor Luigi Barchi, Secretario Generale, Giornate Mediche Internazionali, Pescheria Vecchia 6, Verona, Italy.

Cancer Congress

The 5th International Congress of Scientific Research and Social Struggle against Cancer will be held in Paris at the Sorbonne on July 15–22 under the presidency of Professor A. Lacassagne, director of the Radium Institute of Paris. The sessions will begin on Monday, July 17. In conjunction with the congress the following events will take place in Paris between July 12 and 22: (1) The meeting of the International Cancer Research Commission (the Scientific Committee of the Union) on July 12–13. (2) The General Assembly of the Executive Committee of the Union Internationale contre le Cancer on July 14–22. (3) The celebration of the jubilee of the discovery of radium, Sunday, July 16, the day of the opening of the congress. All requests for information should be addressed to the secretary-general, Professor V. Le Lorier, 6, Avenue Marceau, Paris, 8.

Medical History

Professor R. Shryock, director of the Institute of the History of Medicine, Johns Hopkins University, Baltimore, will give an address on "Social Medicine in the Nineteenth Century" to the Medical Section of the Library Association at Chaucer House, Malet Place, London, W.C.1, on Monday, June 19, at 7 p.m. Tea at 6.30 p.m. Medical men are cordially invited.

Amoebiasis

An International Congress on "Amoebiasis and Other Intestinal Parasitic Conditions in the Adult and Child" will be held at the Spa of Chatel-Guyon, Auvergne, on September 15–16 under the presidency of Professor Chabrol. The honorary president will be Sir Philip Manson-Bahr. Full information may be obtained from the general secretary, Grands Thermes, Chatel-Guyon, Puy de Dôme, France.

1951 Congress of Industrial Medicine

The 10th International Congress of Industrial Medicine will be held at Lisbon on September 9–15, 1951. The president of the organizing committee is Dr. Alex. Ribeiro da Cunha, and the general secretary is Dr. Luis Guerreiro. Full information may be obtained from the latter at Service de Relations Internationales, Institut National du Travail et de la Prévoyance, Praca de Comercio, Lisbon.

Gerontology

The First International Conference of Gerontological Societies will be held at Liége, Belgium, July 9–12. The conference is sponsored by the British, American, and Belgian Gerontological Societies. The chairman of the Organizing Committee is Professor L. Brull, Hôpital Bavière, Liége, Belgium. The delegates of the British Society for Research on Ageing are Professors E. C. Dodds (chairman of the delegation), J. B. Duguid, R. E. Tunbridge, and Drs. M. Critchley and V. Korenchevsky. In addition to the presentation and discussion of the results of gerontological research, it is the purpose of this conference to establish an International Union of Gerontological Societies and to promote the financing of research in this subject throughout the world. Information may be obtained from Professor L. Brull.

Chiropodists' Conference

The annual convention of the Society of Chiropodists will be held at Friends House, Euston Road, London, N.W., on June 22, 23, and 24, under the presidency of Mr. John H. Hanby. The convention will be opened by Sir Cecil Wakeley, P.R.C.S., on June 22, at 2.30 p.m., and the programme includes addresses by members of the medical profession, as follows: June 22, 3.30 p.m., Dr. I. L. MacKinnon, "The Role of the Nervous System in the Life of the Lower Limb"; June 23, 10 a.m., Dr. J. T. Aitken, "Posture in Relation to Feet"; June 24, 9.30 a.m., Mr. J. C. R. Hindenach, "Orthopaedic Aspects of the Rheumatic Diseases in Relation to the Leg and Foot."

Occupational Therapy

An exhibition and garden party will be held at the Occupational Therapy Centre and Training School, 12–14, Merton Rise, Hampstead, London, N.W., and at the annexe, 22, St. John's Wood Park, London N.W., on Friday and Saturday, June 16 and 17, from 3 to 5 p.m.

Medical Women's Federation

The London Association of the Medical Women's Federation has been asked to extend hospitality to the women delegates at the International Radiological Congress to be held in London in July. For this occasion a tea party is being held at the Royal Free Hospital School of Medicine, 8, Hunter Street, London, W.C., on Wednesday, July 26, at 4.30 p.m. Members wishing to attend should notify the honorary secretary, Dr. Margaret M. C. Louden, 5, Wapping Pierhead, London, E.1, before July 1.

SOCIETIES AND LECTURES

A fee is charged for attending lectures marked ●. Application should be made first to the institution concerned.

Monday

EDINBURGH UNIVERSITY.—At Physiology Lecture Theatre, University New Buildings, Teviot Place, June 19, 5 p.m., *"The Medical Man in Literature,"* by Dr. Douglas Guthrie.

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—June 19, 5.30 p.m., *"The Anatomy of the Lacrimal Apparatus,"* by Dr. F. Stansfield.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—June 19, 5 p.m., *"The Natural History of Surgical Infection,"* Moynihan Lecture by Professor F. M. Burnet, F.R.S.

UNIVERSITY COLLEGE (Physiology Theatre), Gower Street, London, W.C.—June 19, 4.45 p.m., *"Genetics and Biochemistry,"* by Professor J. B. S. Haldane, F.R.S.

Tuesday

CHADWICK PUBLIC LECTURE.—At Royal Sanitary Institute, 90, Buckingham Palace Road, London, S.W., June 20, 2.30 p.m., *"The Engineer in Public Health,"* by Professor G. M. Fair (Harvard University).

EDINBURGH POSTGRADUATE BOARD FOR MEDICINE.—At Anatomy Lecture Theatre, University New Buildings, Edinburgh, June 20, 5 p.m., *"The Parietal Lobe,"* by Dr. Macdonald Critchley.

INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—June 20, 5 p.m., *"Varicose Conditions of the Lower Limb,"* by Mr. A. K. Monro.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, London, W.C.—June 20, 4.30 p.m., *"Stenosis of the Larynx,"* by Mr. V. E. Negus.

KENT PAEDIATRIC SOCIETY.—At Broomhill Bank School for Subnormal Children, Rusthall, Tunbridge Wells, Kent, June 20, 2 p.m., meeting.

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, London, S.W.—June 20, 5 p.m., *"Degeneration, Necrosis, and Fibrosis in the Liver,"* Humphry Davy Rolleston Lecture by Professor J. H. Dible.

Wednesday

BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, London, W.—June 21, 8 p.m., ordinary meeting. *"Clinical Problems in Small Intestinal Physiology,"* Twenty-seventh Mackenzie Davidson Memorial Lecture by Dr. Ross Golden (New York, U.S.A.).

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—June 21, 5.30 p.m., *"The Interpretation of the Spectral Sensitivity Curve,"* by Dr. L. C. Thomson.

ROYAL EYE HOSPITAL, St. George's Circus, London, S.E.—June 21, 5 p.m., *"Ptosis,"* by Mr. L. H. Savin.

Thursday

EDINBURGH UNIVERSITY.—At Physiology Lecture Theatre, University New Buildings, Teviot Place, June 22, 5 p.m., *"Social Medicine in the Nineteenth Century,"* by Professor R. Shryock (Baltimore, U.S.A.).

INSTITUTE OF NEUROLOGY: NATIONAL HOSPITAL, Queen Square, London, W.C.—June 22, 5 p.m., *"Meningeal and Radicular Metastases from Cerebral Tumour, especially Pinealomata,"* by Professor Th. Alajouanine (Paris).

MEDICO-LEGAL SOCIETY.—At 26, Portland Place, London, W., June 22, 8.15 p.m., *"Developments in the Law of Divorce and Nullity of Marriage,"* by Mr. William Latey, K.C.

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, London, S.W.—June 22, 5 p.m., *"Degeneration, Necrosis, and Fibrosis in the Liver,"* Humphry Davy Rolleston Lecture by Professor J. H. Dible.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—June 22, 5 p.m., *"Dry Bones,"* Erasmus Wilson Demonstration by Mr. P. H. Mitchiner.

ROYAL EYE HOSPITAL, St. George's Circus, London, S.E.—June 22, 5.30 p.m., *"Retrolental Fibroplasia,"* by Mr. R. P. Crick.

ROYAL SOCIETY, Burlington House, Piccadilly, London, W.—June 22, 8.30 p.m., Conversazione.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—June 22, 4.30 p.m., *"Neurology,"* lecture-demonstration by Dr. A. Feiling.

ST. JOHN'S HOSPITAL DERMATOLOGICAL SOCIETY.—At Royal Society of Medicine, 1, Wimpole Street, London, W., June 22, 4.30 p.m., *"Cute et carne me induisti,"* Prosser White Annual Oration by Professor H. A. Harris.

Friday

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—June 23, 5.30 p.m., *"Causes of Blindness,"* by Dr. J. Marshall.

MAIDA VALE HOSPITAL FOR NERVOUS DISEASES MEDICAL SCHOOL, Maida Vale, London, W.—June 23, 5 p.m., clinical neurological demonstration by Dr. P. H. Sandifer.

APPOINTMENTS

BROWN, ARTHUR E., M.B., B.S., D.P.H., Medical Officer of Health, Diss and Wymondham Urban District Councils, Depwade and Loddon Rural District Councils, and Assistant County Medical Officer, Norfolk.

COHEN, E. LIPMAN, M.B., B.CHIR., Dermatologist (Consultant), St. Margaret's Hospital, Epping, Essex.

COLEMAN, J. S., M.B., B.S., D.P.H., Medical Officer of Health, County Borough of East Ham.

CROSS, COCHRAN, M.B., Ch.B., D.P.H., Medical Officer of Health for the County of Orkney and Group Hospitals Officer, the Orkney Hospitals.

DURAND, R. W., M.R.C.S., L.R.C.P., Superintendent-in-Chief, Wellington Hospitals Board, Wellington, New Zealand.

HARTSTON, WILLIAM, M.D., M.R.C.P., D.T.M., D.P.H., Senior Medical Officer, London County Council.

KING'S COLLEGE HOSPITAL, Denmark Hill, London, S.E.—*Assistant Physician to Children's Department*, Mary J. Wilmers, M.D., M.R.C.P. (Dr. Wilmers was appointed Assistant Physician to the Children's Department in June, 1948, and *not* First Assistant as stated in this column in the *Journal* of May 13 (p. 1154).)

LIVERPOOL REGIONAL HOSPITAL BOARD.—*Consultant Psychiatrist (whole-time) to Rainhill Hospital*, W. A. M. Robinson, M.B., Ch.B., D.P.M.; *Consultant Radiotherapist (whole-time) to Liverpool Radium Institute*, W. J. L. Francis, Ch.M., F.R.C.S., M.Rad., D.M.R.T.; *Consultant Radiologist to hospitals in Wirral*, G. D. Scarrow, M.B., Ch.B., M.Rad., D.M.R.D.; *Consultant Venereologist (whole-time) for duties in Liverpool and clinics in Warrington and St. Helens*, D. Goldstein, M.D.; *Assistant Senior Medical Officer*, R. Glyn Thomas, M.B., Ch.B., D.P.H.

MINNS, WILSON, M.B.E., T.D., M.B., B.S., D.P.H., B.Hy., Deputy County Medical Officer, Northumberland County Council.

PRICE, PIERS B. W., M.B., Anaesthetic Registrar, Royal Infirmary, Worcester.

ROBERTSON, DONALD NORMAN STRUAN, M.B., Ch.B., M.R.C.O.G., Consultant Obstetrician and Gynaecologist, Aylesbury and High Wycombe Region.

ROUGHEAD, JOHN A., M.D., D.P.H., Medical Officer of Health for Ayr County.

ST. ANDREW'S HOSPITAL, Devons Road, London, E.—*Senior Registrar Anaesthetist*, W. A. Groom, L.M.S.S.A., D.A. *Obstetric and Gynaecological Registrar*, Monica M. A. Murphy, M.B., Ch.B., D.Obst.R.C.O.G.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Brennan.—On May 19, 1950, at Queen Charlotte's Maternity Hospital, London, W., to Betty, wife of Squadron Leader T. N. N. Brennan, a daughter.

Hopkins.—On May 30, 1950, at Foresterhill, Aberdeen, to Betty, wife of Ian B. Hopkins, M.B., Ch.B., Riversfield, Elion, Aberdeenshire, a son.

Hughes.—On June 8, 1950, at Bristol Maternity Hospital, to June (formerly Kingan), wife of Dr. E. Brierley Hughes, a daughter.

Scriven.—On June 6, 1950, at Gally Hill Nursing Home, Church Crookham, Hants, to Dr. Jeanne Scriven (formerly Edwards), wife of Dr. W. H. Scriven, M.B.E., F.F.A. R.C.S., a daughter.

Short.—On May 23, 1950, at Chuanchow, Fukien, China, to Dr. Jean H. Short (formerly Merry), wife of Mr. Douglas W. Short, F.R.C.S.Ed., twin daughters

Slovick.—On June 4, 1950, at King's College Hospital, Denmark Hill, London, S.E., to Pamela, wife of Dr. David Slovick, a daughter.

DEATHS

Galloway.—On June 5, 1950, Robert Menzies Galloway, M.D., D.P.H., Medical Officer of Health, Bolton, of 10, Stapleton Avenue, Bolton, husband of Margaret Galloway, M.B., Ch.B.

Gibbons.—On June 4, 1950, at Lee-on-Solent, James Barry Gibbons, L.R.C.P.&S.I. Lieutenant-Colonel, I.M.S., retired, aged 91.

Gilchrist.—On June 4, 1950, at Vachery, Shere, Surrey, John Gilchrist, M.D., late of 2, Somerset Place, Glasgow.

Logie.—On June 5, 1950, at Lower Warwick House, St. Mary Bourne, Andover, Hants, Henry Burton Logie, M.D., aged 67.

Lyons.—On June 1, 1950, at The Manor House, Greetwell Road, Lincoln, James Lyons, M.D., F.R.C.S.Ed.

McKendrick.—On June 5, 1950, the result of a climbing accident, John Wellesley McKendrick, M.B., Ch.B.

Mackenzie.—On June 3, 1950, at Higher Stratton, Chalfont St. Giles, Bucks, Donald Francis Mackenzie, D.S.O., M.B., Ch.B., Colonel, late R.A.M.C., retired.

Macleod.—On May 13, 1950, at Hetton-le-Hole, Co. Durham, Roderick Macleod, M.B., Ch.B., D.P.H.

Meaden.—On May 26, 1950, at the Presbytery, Thetford, Charles Anderson Meaden, M.R.C.S., L.R.C.P.

Michael.—On June 2, 1950, at Manor Lodge, Manor Park Gardens, Edgware, Middlesex, George Coleman Michael, M.R.C.S., L.R.C.P., aged 58.

Newlands.—On June 2, 1950, at 25, Beechgrove Avenue, Aberdeen, Bethia Muir Newlands, M.B., Ch.B., D.P.H.

Parrett.—On May 27, 1950, at 49, King Street, Thorne, near Doncaster, Edward Erratt Parrett, M.R.C.S., L.R.C.P., aged 77.

Paxton.—On June 4, 1950, at Folkestone, William Thompson Wotherspoon Paxton, M.D., of 16, Clifton Gardens, Folkestone.

Phillips.—On June 9, 1950, at 696, Pinner Road, Pinner, Middlesex, Albert Edward Phillips, M.B., B.Ch., Surgeon Commander, R.N., retired, formerly of 4, Crofton Terrace, Dun Laoghaire, Co. Dublin.

Porter.—On June 4, 1950, at Faversham, Kent, Herdman Porter, M.B., Ch.B., aged 74.

Porter.—On June 4, 1950, at St. Annes, Jehidy Terrace, Falmouth, Frederick Joseph William Porter, D.S.O., M.R.C.S., L.R.C.P., Major, R.A.M.C., retired, aged 84.

Potts.—On May 25, 1950, at 13, Euston Road, Great Yarmouth, Horace Potts, M.R.C.S., L.R.C.P., aged 79.

Slater.—On June 3, 1950, at St. Bartholomew's Hospital, Alan Butler Slater, M.D., of 87, Chiltern Court, London, N.W., aged 75.

Tatton.—On May 29, 1950, at 5, Napier Road, Edinburgh, Glyde Philip Tatton, M.B., B.S.

Wall.—Recently, Hugh Alton Chandos Wall, M.B., of Coraki, N.S.W., Australia.

Wigg.—On April 22, 1950, at Aldgate, South Australia, Henry Higham Wigg, M.D., F.R.C.S.Ed., aged 92.

Wilson.—On June 7, 1950, at The Chase, 21, Eastcote Road, Ruislip, Middlesex, Wilfrid Max Wilson, M.R.C.S., L.R.C.P., aged 53.

Woolicombe.—On June 9, 1950, at Okehampton, Devon, Alfred Woolicombe, M.R.C.S., L.R.C.P., D.P.H., Surgeon Captain, R.N., retired.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Protamine Zinc Insulin

Q.—*Is it possible or advisable to control diabetes with protamine zinc insulin alone? If so, what is the right time for the injection? The maximum effect is said to take place in 12 to 24 hours. Is this correct?*

A.—Provided that the patient has a relatively mild and stable type of diabetes, protamine zinc insulin can safely be used alone. It should be given half an hour or so before breakfast, but the carbohydrate should be arranged differently. If the carbohydrate allowance is 150 g., the carbohydrate ration at the three meals (breakfast, lunch, and tea) should be 30 g.; the evening meal should contain 50 g., and 10 g. should be given at bedtime. The same proportion should be used for larger amounts of carbohydrate. The dose of insulin may be as high as 40 units, but it is unwise to give larger amounts. If the dosage of insulin is sufficient, the urine after breakfast and until before the midday meal will probably contain some sugar, but the urine during the rest of the day and before breakfast should be sugar-free.

If the blood sugar is within normal limits, say below 150 mg. per 100 ml. before breakfast, but high before the midday meal, say over 200 mg. per 100 ml., it is advisable to use some of the ordinary quick-acting insulin, say 5 units. This can be given as a separate injection, but if it is desired to give the two insulins by the same injection considerable changes must be made. The protamine zinc insulin contains a good deal of "free" protamine which will convert the ordinary insulin into protamine zinc insulin. The amount of ordinary insulin must be slightly greater than the P.Z. to obtain any "quick" action. If the dose of P.Z. is 20 units it should be reduced to 10 units and 12 units of the ordinary insulin given in the same injection. The finding of the correct proportion of the two insulins may present some difficulties, and here it is often better to admit the patient to hospital so that the change can be controlled by estimations of the blood sugar.

Tuberculosis of the Bronchi

Q.—*How is the diagnosis of tuberculosis of the bronchi made?*

A.—Tuberculosis of the trachea and bronchi is almost always found in association with pulmonary tuberculosis. Features which suggest a bronchial lesion include the occurrence or persistence of a positive sputum without obvious cause radiologically: signs of bronchitis, including persistent rhonchi, cough with frothy sputum and wheezing; cough, sputum, and fever out of proportion to the apparent disease in the lungs; and radiological evidence of lobar or segmental collapse. The diagnosis can be confirmed only by bronchoscopy.

Mosquito Bites

Q.—*What is the best palliative treatment for mosquito bites, and how should one treat the large blisters caused by the bite of Aëdes vexans?*

A.—Although much progress has been made with mosquito repellents—for example, dimethyl phthalate—there is little that can be done to prevent the irritation caused by the bites of mosquitoes such as *Aëdes vexans*. The local application of antihistamines is of very doubtful value, and reliance must be placed on the old-fashioned remedies—sodium bicarbonate solution or calamine lotion. Some of the proprietary analgesic ointments may give temporary relief, especially in children.

Immunization against Tetanus

Q.—*A horse has recently contracted tetanus. It never leaves the farm. The stable is 50 yards from the farmhouse, where the farmer and his wife, their son aged 1 year, and one maid live. There is no history of previous tetanus on the farm. Is immunization advisable for the farmer and his family?*

A.—Most domestic animals—horse, cow, sheep, dog, poultry—and also vermin may harbour tetanus spores in the gut, so that any manured soil or the dust of streets or farmhouses is likely to contain these spores, and the occurrence of tetanus in a farm horse is an accidental happening of no special significance. The incidence of tetanus in man is very low in this country (deaths number less than 200 per annum), although there is a slight occupational hazard among gardeners and farm workers. While the risk, therefore, to any family living on a farm is minimal, it is easy to take preventive measures by active immunization with tetanus toxoid. Two 1-ml. injections at an interval of six weeks or more will ensure a good basic immunity which can be boosted by a further injection a year or so later.

Sodium Amytal

Q.—*Are there any contraindications to the prolonged use of sodium amytal (over a period of years) especially with regard to its effect on the liver?*

A.—Sodium amytal is a short-acting barbiturate, being rapidly broken down and detoxicated in the body, probably by the liver. Provided advanced hepatic disease is not present there is little danger of therapeutic doses producing cumulative poisoning even though its use is continued regularly for years, though some tolerance and mild addiction are likely to occur. Sodium amytal is most unlikely to have a detrimental effect on the liver. Occasionally patients become sensitive to barbiturates and in consequence develop erythematous skin rashes and drug fever.

Iron for Anaemia

Q.—*A female patient, aged 37, has suffered from anaemia of varying degree since May, 1937, when she developed a severe metropathia haemorrhagica. The patient was married later that year but failed to become pregnant. Laparotomy was performed in March, 1940, and many small cysts of the ovaries were ruptured. In October, 1941, laparotomy was again performed and a lobulated intramural fibroid was removed. Following this, menstruation became more satisfactory though not entirely regular. Pregnancy was achieved in May, 1944, and by June the blood picture was dramatically changed and the haemoglobin was 100%, where it remained until a healthy female infant was born in February, 1945. In March of that year the haemoglobin dropped to 70%. There was a pregnancy again in October, 1946, and once more the haemoglobin level returned to between 90 and 100%, where it remained until a healthy female child was born in August, 1947, when the haemoglobin dropped to 71%. In October, 1948, she had an abortion at three months with very severe loss requiring a whole-blood transfusion. In January, 1949, the patient again became pregnant, but the haemoglobin remained at no more than 70% throughout. The child born in October was a large healthy male. The present blood picture shows: 3,850,000 red blood cells, haemoglobin 60%. Why should the two female foetuses be associated with a normal blood count but not so the male? The patient obviously needs iron, but none of the many preparations tried through these years has been tolerated. All produce a most violent diarrhoea. I should welcome any suggestions on this point.*

A.—It appears certain that this patient has a relapsing hypochromic anaemia due to deficiency of iron. Although there is a history of menorrhagia and blood loss from abortion, it is unwise to assume that no other source of haemorrhage exists; indeed, from the data it sounds as though uterine bleeding was insufficient to explain the repeated relapses. For this reason it would be advisable to examine the stools for occult blood

and to exclude haemorrhoids by means of proctoscopy. If there is any loss of blood into the alimentary tract it will require appropriate treatment.

In addition to controlling all sources of haemorrhage amenable to control, it is clear that the patient needs iron. There are undoubtedly some individuals who are unable to take any iron preparation by mouth, but such idiosyncrasy is rare. One of the preparations of colloidal ferric hydroxide is worth a trial if it has not already been used. A start should be made with 30 gr. (2 g.) three times daily, and the dose gradually raised until it has reached 2 drachms (8 g.) three times daily. It is less likely to cause gastro-intestinal symptoms than any other preparation. If the patient cannot tolerate iron by mouth in this form, there is no alternative to intravenous administration. "Ferrivenin" may be used; the total quantity of iron required may be estimated by allowing 25 mg. for each rise of 1% haemoglobin desired, an additional 750–1,000 mg. being given to replenish the storage depots. The initial dose should be 1 ml. (20 mg. of iron); if no reaction ensues it should be followed by 2 ml., 5 ml., and 10 ml. It is advisable to limit the maximum individual dose to 10 ml. (200 mg. of iron). Injections may be given daily until the required quantity of iron has been administered. The variations in the patient's blood counts during her pregnancies cannot reasonably be attributed to the sex of the foetus; other factors, so far undiscovered, must have been operative.

Infantile Hemiplegia

Q.—*A male child, now aged 8, had a sudden onset of infantile hemiplegia at 15 months. Following a convulsion and after remaining in status epilepticus for four days, he was discovered to have a left-sided hemiplegia. He made a quick and fairly good recovery, but he still has a "hemiplegic" leg on the left side. When he was 6 he started to have Jacksonian convulsions in the paralysed side. These occur at night about once in every three months. His intelligence seems unimpaired except for mild behaviour disorders. What is the prognosis in this case? What are the prospects regarding surgical treatment of his epileptogenic focus?*

A.—It is probable that this child's original illness was a cerebral venous thrombosis. As regards the prognosis, it is unlikely that there will be further improvement in the hemiparesis, as nearly seven years have elapsed since the initial illness. In many cases of this type the epileptic attacks respond to regular and prolonged treatment with phenobarbitone and sodium diphenyl-hydantoinate, but, if attacks persist in spite of this, surgical treatment would have to be considered. Before any useful opinion on the possible benefit to be expected from operation could be given, an electroencephalogram and an air encephalogram would be necessary to help in assessing the degree and location of cerebral damage.

Nasal Folliculitis

Q.—*What treatment is advised for a male patient, aged 51, troubled with a heavy growth of hairs in the nostrils? These, like his scalp hair, are thick and wiry; they cause irritation and sometimes boils. On one occasion I believe a hair perforated the ala nasi. He also suffers from renal glycosuria and is subject to boils elsewhere. Ung. hydrarg. ammon. dil. 2½% is used as a prophylactic from time to time. Is any other, perhaps more radical, treatment advised?*

A.—The condition described is known to all dermatologists. The follicle of very stiff bristly hairs within the nose can be infected with staphylococci of several types, and a perforating folliculitis follows. Presumably the infection is conveyed by, and aggravated by, the fingers touching the region. Ung. hydrarg. ammon. dil. is usually effective; or ung. hydrarg. nit. dil. and ung. zinci oxidi—equal parts of each. If the patient does not refrain from touching the area, the hairs may have to be destroyed by electrolysis or diathermy. If there are boils elsewhere, a vaccine may assist obstinate cases. The general health must be considered, and in view of the renal glycosuria the diet should be regulated.

Emergency Method for Estimating Blood Sugar

Q.—*After reading the article on a "Simple Emergency Method for Estimation of Blood Sugar" (August 20, 1949, p. 418), I am anxious to have the exact description of the solutions used in this method.*

A.—*Alkaline copper reagent:* Solution A.—13 g. $CuSO_4.5H_2O$ are dissolved in water and the volume made up to 1 litre. Solution B.—50 g. $NaHCO_3$ are dissolved in a beaker by stirring in the minimum amount of distilled water (about 700 ml.). When all the bicarbonate is dissolved, 40 g. anhydrous Na_2CO_3 is added while continuing to stir the solution. When the carbonate has dissolved, a solution of 36.8 g. potassium oxalate in 120 ml. of warm water is added to the mixture. Finally a solution of 24 g. sodium potassium tartrate in the minimum amount of water (about 100 ml.) is added. The mixture is poured and washed into a 1-litre volumetric flask, the volume is made up to the mark, and the solution well shaken.

The copper reagent used is prepared freshly each day and is a mixture of exactly equal volumes of solution A and B.

Phosphomolybdic Acid Reagent (Folin and Wu, 1920): 35 g. molybdic acid and 5 g. sodium tungstate are dissolved in 250 ml. of 2n-NaOH and the solution boiled for 30 minutes. Water is added to about 350 ml., followed by 125 ml. of 89% H_3PO_4 (sp. gr. 1.75), and the volume made to 500 ml.

Isotonic Sodium Sulphate—Copper Sulphate Solution: A mixture of 320 ml. of 3% sodium sulphate ($Na_2SO_4.10H_2O$) and 30 ml. of 7% $CuSO_4.5H_2O$.

Sodium Tungstate: 10 g. per 100 ml.

NOTES AND COMMENTS

Chinese Geese and Salmonella.—D. F. F. CARTWRIGHT (Sevenoaks, Kent) writes: I cannot agree with the somewhat optimistic view advanced by the expert who answered a question upon this subject (June 10, p. 1382). Perhaps my own experience may be of some interest. A pen of three geese and a gander was raised from pure-bred Chinese eggs in April, 1949. There was no trouble until January, 1950, when the four birds, which had been kept in a dry paddock close to a rat-infested chicken-house, suddenly became ill; one goose died, but the remaining two geese and the gander recovered. Unfortunately, we were away at the time; the incident was reported to us by the gardener on our return, and we put the illness down to some poison that the birds had picked up, and did nothing further in the matter. In March, 1950, the birds were moved about five miles to our present house; shortly afterwards one of the geese became broody and was set upon five eggs of our own rearing and four pure-bred Embdens from a neighbour. Six goslings, three of our own and three Embdens, were hatched out. Since then, we have lost two Embdens and two of our own from acute salmonella infection, proved by post-mortem examination. What has happened is obvious. The geese became infected from the rats upon our original ground and one of the surviving geese has become a carrier. Until we eliminate this carrier, we cannot breed, nor eat, nor sell our eggs. It must be remembered that Chinese geese, unlike the heavy breeds, are primarily water birds and are grazers. It will be very difficult for your correspondent to keep his birds away from water, and it would be still more difficult for him to keep his rats away from the birds. The excreta of a rat infected with *Salmonella typhi-murium* might lie unobserved in the grass close to his pond, and infect his geese, even though the birds had no direct access to the water. Whether or no the eggs of geese become infected is a matter of argument among veterinary surgeons. Cultures are at present being made from my goose eggs, and I shall be pleased to advise you of the results in due course, if the matter appears to be of interest. Meanwhile, I would very strongly advise your correspondent to think again before he embarks upon the rearing of any form of goose in rat-infested premises.

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